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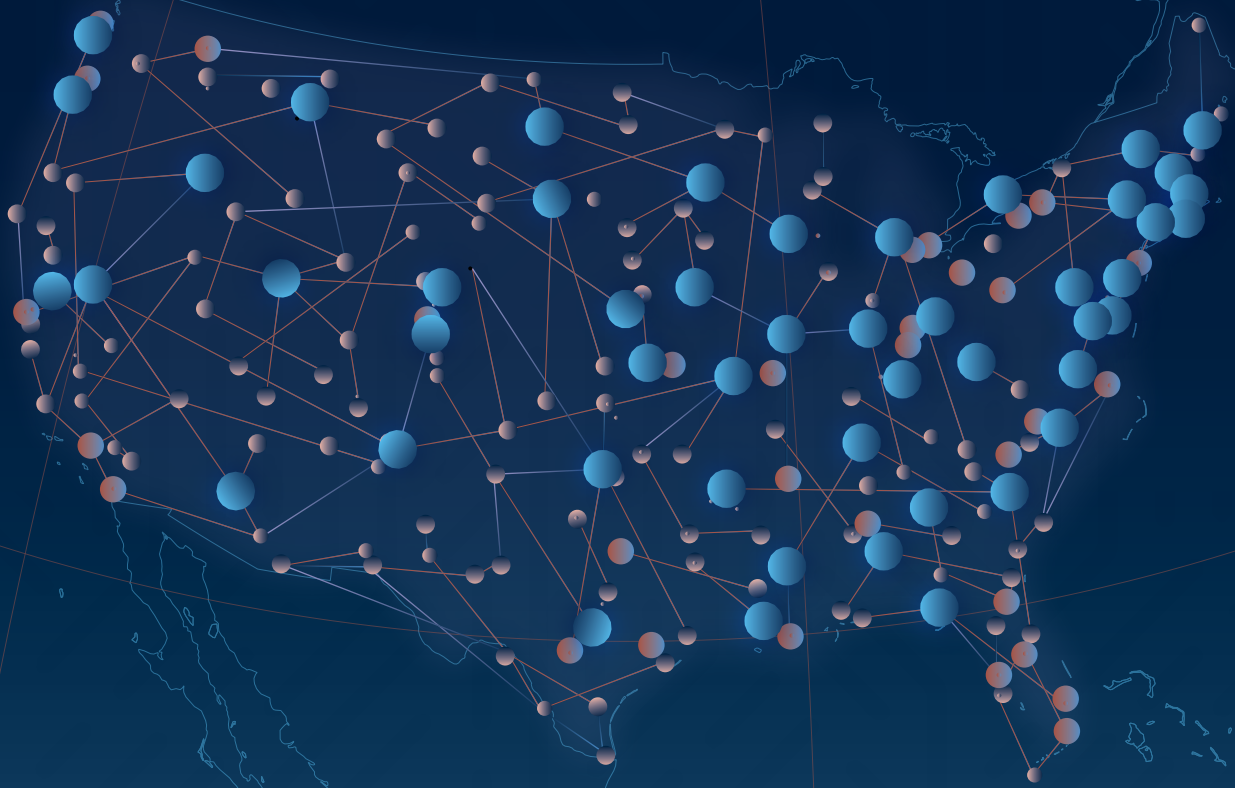
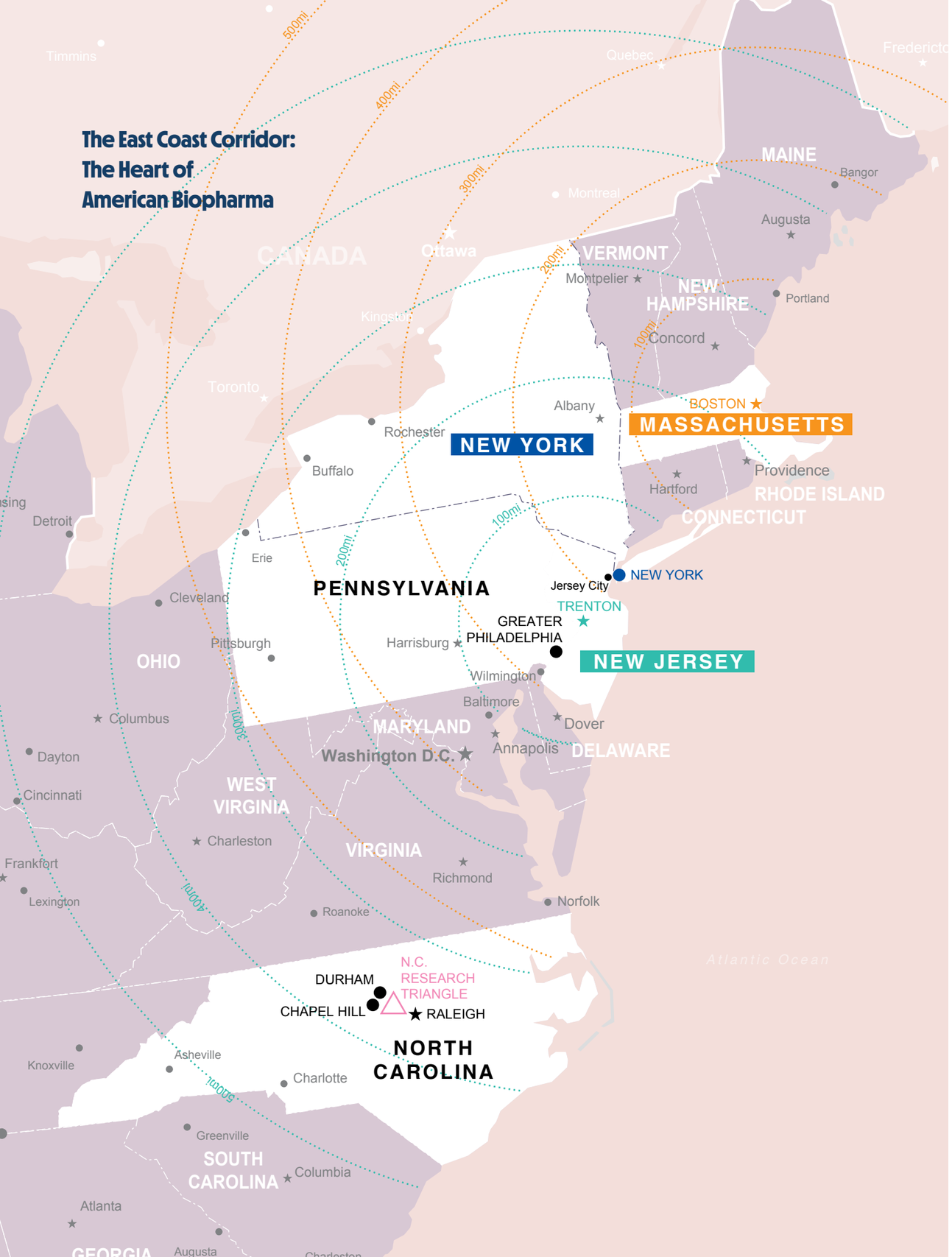


# UNITED STATES LIFE SCIENCES 2022

Funding and Regulatory Climate - Drug Discovery - Contract Services - Hubs and Academia - Artificial Intelligence




# Dear Reader,

Welcome to the 2022 edition of the United States Life Sciences Industry Report.

After two years of fighting Covid-19, the United States has offered a glimpse of what the industry may look like in a post-pandemic world. Compared with the investment frenzy that led to a peak in capital inflow into the industry in early 2021, the financial climate has cooled considerably. The ensuing period of dramatic correction has forced companies to work harder to prove their worthiness of investors' dollars. Within this context, it is increasingly small and mid-sized companies claiming ownership to the development pipeline and commercialization of new drugs. Tireless advances have been made across a variety of fields, such as gene editing and cell-based therapies, as well as in the introduction of novel drug delivery platforms and diagnostics tools. These efforts culminated in 50 new drug approvals in 2021, in line with the past five years of consistently strong output.

Of course, the magnitude of success does not rest squarely on the shoulders of only pharmaceutical and biopharmaceutical companies – contract service providers are crucial to the health of the life sciences ecosystem. Responding to the heightened complexity of the field, the explosion of streamlined companies with modern in-house manufacturing capabilities, and an industry-wide rallying cry for increased domestic production, CROs and CDMOs are stepping up to create a more robust environment.

The following pages bring together insights from interviews conducted with over 80 industry leaders whose experiences collectively span all areas of the sector. We would like to warmly thank these executives and researchers whose thoughtful contributions were invaluable to the report as well as our association partners at BioNJ and Biocom California. We hope that you enjoy reading our 2022 edition of the United States Life Sciences Industry Report.

**Alfonso Tejerina**
General Manager and Director,
Global Business Reports
(GBR)

## Introduction to USA Life Sciences

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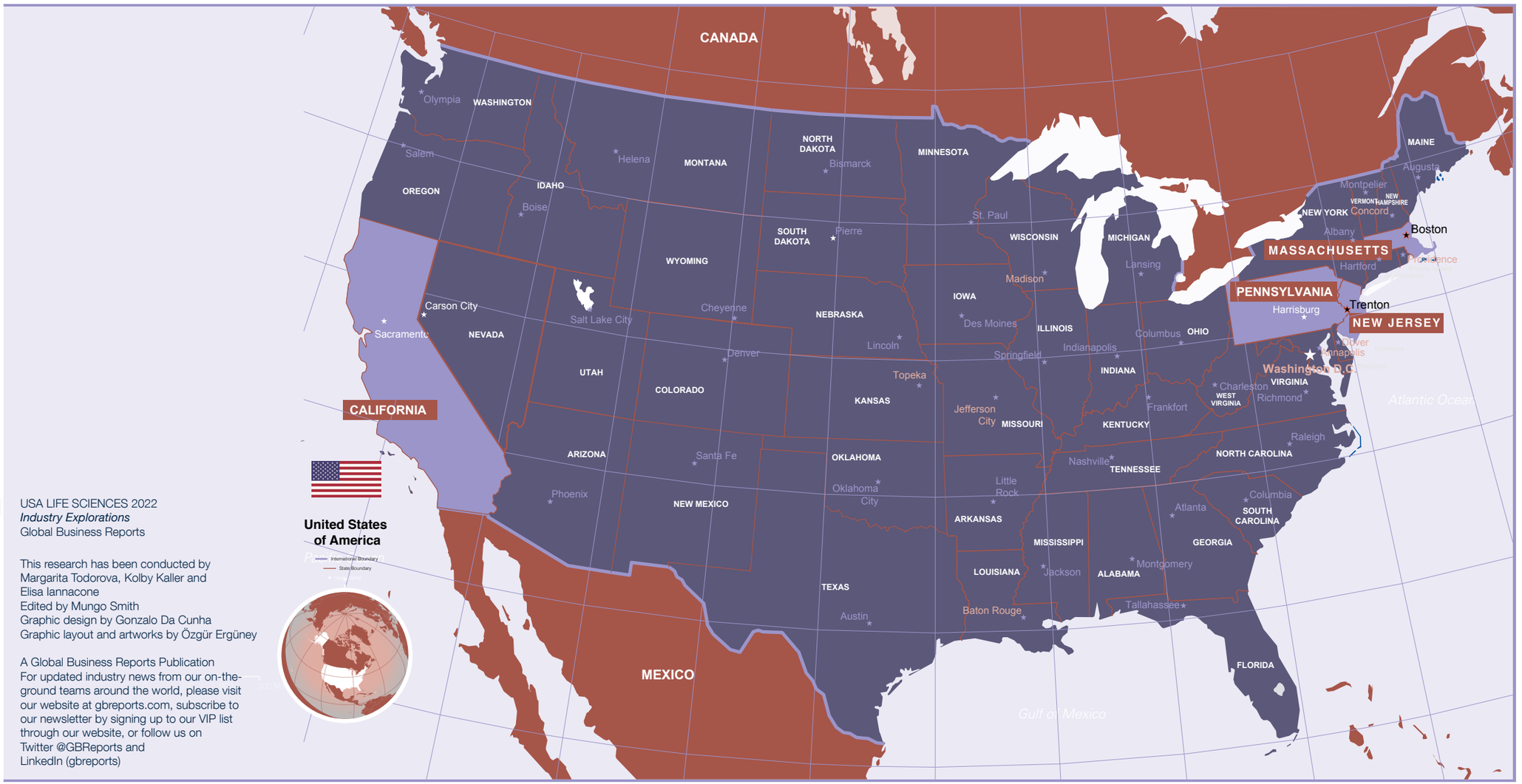


**United States of America**

International Boundary
State Boundary




USA LIFE SCIENCES 2022
*Industry Explorations*
Global Business Reports

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# INTRODUCTION TO USA LIFE SCIENCES

"The industry's response to Covid-19 was unprecedented - bringing a vaccine to market in record time. Companies developed revolutionary therapies to curb the severity of SARS infection, and new diagnostics continue to enter the market. It is an enormous understatement to say the industry changed the world."

**– Joe Panetta,**
**President & CEO,**
**Biocom California**



Image courtesy of Vedanta Biosciences

# Introduction to USA Life Sciences

## The end of an era?

The achievements of the life sciences industry over the past two years have been nothing short of astounding. In a previously unimaginably short time frame, the sector developed and produced multiple Covid-19 vaccines that were effectively distributed to billions of people across the globe. Simultaneously, revolutionary therapies to curb the severity of infection and a host of new diagnostics tools were introduced.

Rather than celebrating a singular entity – whether it be a pharma or biotech company, a research institution, or even an administration – it is instead a particular ethos that carried the day: the willingness to collaborate. A DNA map of the virus was distributed around the world to enable efficient collaboration in discovering vaccines. According to Anne Pritchett of PhRMA, voluntary partnerships around the world led to over 370 collaborations for Covid-19 vaccine manufacturing and 155 for therapeutics, including longstanding intellectual property protections and voluntary technology transfers. Partnerships between industries and governments were also significant: The US government invested US$13 billion into the development of vaccines, and the FDA accelerated its regulatory review process without sacrificing quality to meet the emergency.

Yet the driver of this collaboration was a common enemy: the Covid-19 virus. Individual motives took a backseat to an issue in which all stood to gain or lose collectively. With this in mind, a question naturally arises – once the pandemic is over, will everybody go home?

Juliet Hart, CEO and founder of Hart & Chin, believes this will be the case. "Once this period is over, companies will no longer be unified by the same goal, and competition will resume," Hart predicts. "The experience has made some people wonder what it would look like if the industry came together to solve cancer in the same way it came together around Covid-19, but science is not simple and collaboration is even harder."

Nevertheless, the past two years have created and strengthened bonds between unlikely actors who may not be so quick to forget what they can achieve when working together. While collaboration may be challenging, this period has proven that life sciences companies are more than up to the task. That is not a lesson that will likely be so quickly unlearned.

> The experience has made some people wonder what it would look like if the industry came together to solve cancer in the same way it came together around Covid-19, but science is not simple, and collaboration is even harder.
>
> **– Juliet Hart, CEO & Founder, Hart & Chin**

**The popularity of the life sciences**

Covid-19 presented a much-needed facelift to the reputation of the life sciences industry. Public opinion reached an all-time high, as people witnessed for the first time in recent history what it is like to live with a global unmet medical need. As vaccines flew through the development and regulatory processes, the public watched with a keen interest, and in doing so, learned about the groundbreaking achievements being made in fields such as mRNA technology.

In the US, there has historically been a pervading sentiment that pharmaceutical companies are overly profit-driven. The pandemic gave these companies a platform to prove otherwise. AstraZeneca, for example, was not even in the vaccine business before the start of the pandemic. That did not stop their executive leaders from making a decision to pour resources into developing a Covid-19 vaccine, aware that the global need had to be addressed immediately. If leading pharma and biotech companies did not step up, who would? This level of altruism from a public company allowed them, if only momentarily, to shift from "villain" to "hero" in the eyes of many.

At the same time, undercurrents of a war on science came to a boiling point. Spectators and officials began publicly arguing with scientific facts. The lessons learned from this period are messy and contradictory, and it remains to be seen whether in years to come the pandemic will have served as a rallying point around the triumphs of science, or a further solidification of a dividing line between its advocates and disbelievers.

If 2020 was about reaction and 2021 about action, 2022 will be a year of picking up the pieces to create a stronger, more unified force that is better equipped to confront large-scale public health crises that the future holds in store. ■

> Throughout the pandemic, we have seen an unprecedented level of collaboration across the private sector and among public and private sector actors toward a common goal of combatting Covid-19. Biopharmaceutical companies continue to work around the clock to research, develop and produce safe and effective Covid-19 vaccines and treatments to save lives.
>
> **– Anne Pritchett, Senior Vice President of Policy, Research and Membership, PhRMA**





# Kathryn McDonough

Co-Head of Healthcare for Middle Market Banking & Specialized Industries
**J.P. MORGAN COMMERCIAL BANKING**

**Can you provide an update on how 2021 was from J.P. Morgan's perspective, including any initiatives the company took on in the life sciences sector?**

2021 was another banner year for deal making in the life sciences sector. Biopharma therapeutics and discovery platform companies led the way in licensing and venture attraction—while medtech activity remained well above its pre-pandemic levels.

We have a team of relationship bankers and specialists dedicated to the life sciences and healthcare sectors. Our focus continues to be on delivering the full strength of J.P. Morgan's network, capabilities, and resources to help these companies thrive at every stage of growth. We believe in the pivotal contributions these entrepreneurs add to society, shareholders and employees alike.

We provide tailored solutions including day-to-day credit, financing and treasury services, as well as financial solutions offered across other lines of business, including investment banking, wealth management and more.

Through a new collaboration with Dealforma, we are able to provide the industry with broad and deep insights on venture capital, partnerships and funding for high-growth life sciences companies.

**What is your assessment of the current biotech investment landscape?**

The biopharma and medtech deal space has seen several ups—and a few downs—since 2020. Despite market volatility in the first quarter of 2022, many of these changes point to opportunities for life sciences companies to build on their strengths and grow.

What does this mean for the rest of 2022? The pressure is on clinical programs as an already sensitive public market leaves no room for missed scientific milestones and valuation catalysts.

Also, licensing and private fundraising will continue to support early-stage science and company growth given the challenges in M&A exits and IPOs.

**What trends do you see driving the sector forward?**

Following multiple record years for licensing and venture funding, biopharma deal making is off to a slower start in 2022. Most deal categories showed a decline, except for licensing in specific therapy areas, advanced modalities and late-stage venture investment.

Big pharma is in-licensing earlier into discovery and technology platforms. Large-cap biopharma has been signing deals earlier in development since the early 2000s. As high as 90% of deals happened in preclinical and earlier stages in 2019. Q1 2022 has seen much of the same following two years of Covid-related deal making and a recent return to licensing discovery programs.

Large-cap biopharma is doubling up on oncology and neurology across all modalities. Tracking large-cap biopharma's deal activity among therapy areas and treatment modalities is top of mind to all business developers. Most of the top five within each category saw increased upfront cash and equity totals since 2019. ■

**What are the most important initiatives that have been undertaken by Janssen's infectious diseases & vaccines segment within the past year?**
We have been focused on multiple areas in the vaccine space, including RSV, Covid-19, and antimicrobial resistance.
We see an incredible opportunity in the respiratory infection space, including solutions for both Covid-19 and respiratory syncytial virus, or RSV, which affects over 64 million people worldwide per year, yet no vaccines or antiviral treatments currently exist. For our Covid-19 vaccine, we implemented a development plan that studied our vaccine in diverse populations in Asia, Africa, Latin America, the US and Europe. We also made a commitment to make up to 900 million vaccine doses available to the African Union and COVAX Facility, combined, through 2022.

Another area of focus for us is antimicrobial resistance, or AMR, which is one of the top ten threats to global health and is quickly becoming one of the leading infectious disease-related causes of death worldwide. Our investigational extra-intestinal pathogenic E. Coli vaccine candidate (ExPEC9V) is currently in Phase 3 development for the prevention of invasive ExPEC disease.

Finally, we are working on developing a functional cure for chronic hepatitis B as well as focusing on steps that can be taken to mitigate the stigma associated with the disease. We are investigating multiple promising modalities, including combining antivirals with immunomodulators to transform how infectious disease pathogens such as the hepatitis B virus (HBV) are managed by achieving high rates of functional cure.

We developed a long-acting injectable HIV treatment regimen in partnership with ViiV Healthcare to reduce the frequency of treatment. We are currently working to expand our partnership with ViiV Healthcare to explore our long-acting rilpivirine and cabotegravir regimen as both a monthly self-administered regimen and an ultra-long-acting regimen, administered every three months or more.

For influenza, we believe that pre-exposure prophylaxis has the potential to revolutionize the prevention of seasonal respiratory viral infections in the most vulnerable populations.

**In vaccines, we are progressing late-stage programs of break-through vaccines against diseases where vaccines are not currently available, such as RSV and multidrug resistant bacterial infections, including ExPEC and Staphylococcus aureus.**

# Candice Long

President – US Infectious Diseases & Vaccines
**JANSSEN PHARMACEUTICALS**

In antimicrobial resistance, we are targeting multidrug resistant bacterial infections through a variety of approaches, including via CRISPR-Cas3 engineered bacteriophage cocktails, aiming for first-in-class precision medicine in the fight against AMR.

In vaccines, we are progressing late-stage programs of break-through vaccines against diseases where vaccines are not currently available, such as RSV and multidrug resistant bacterial infections, including ExPEC.

**How does Janssen leverage innovative technology for vaccine R&D?**
Our Covid-19 vaccine program leverages Janssen's AdVac technology, which is the same technology used to develop and manufacture Janssen's European Commission-approved Ebola vaccine regimen and to construct both our RSV and HIV vaccine candidates.

Our AdVac technology is based on the development and production of adenovirus vectors, or gene carriers. Adenovirus vectors are genetically altered forms of an adenovirus that lack the DNA needed to replicate, so the vaccine cannot cause a cold. In the case of the Covid-19 vaccine, the immune system of someone who receives our vaccine recognizes the Covid spike protein as foreign once it enters their cells, producing antibodies and activating T cells to target it. This allows the individual's immune system to recognize the SARS-CoV-2 spike protein and be ready to defend against it.

**Could you provide insight into Janssen's recent agreement with Aspen SA Operations and the impact you anticipate this having for Covid-19 relief efforts in Africa?**
The agreement enables the first Covid-19 vaccine to be manufactured and made available by an African company for people living in Africa. Currently only about 12 percent of people in Africa are fully vaccinated, well below the WHO's targets.

**What is your prediction for the long-term impacts that Covid-19 will have on public perception of infectious diseases and the importance of vaccines?**
Covid-19 gave us a close look at our capacity for preparedness and rapid response when an infectious disease outbreak becomes a pandemic. It illuminated the gaps in public understanding about the development and safety of vaccines. We know vaccines can lead to higher quality, longer lives, but wide acceptance and uptake, in addition to an adequate supply chain and access, need to occur for vaccines to be effective for the global community. ■





**What role has digitization played for EY in the past year?**
Our business has seen a positive uplift as we focused on digital initiatives to continue supporting our clients in the life sciences sector. The pandemic has shed light on the importance of digitization and AI, and EY's Smart Reviewer process has received significantly more attention over the past months. This technology solution leverages AI and ML algorithms to automate key activities in the promotional materials' review process. It allows for more efficiency and reliability, ultimately mitigating the challenge of human error and allowing better quality information to enter the market faster, while reducing risks and cutting costs. The solution accelerates the products of our biopharma clients to reach their patients faster.

2021 was a year defined by uncertainty, but EY experienced solid growth, and we have a positive outlook for the future. Our primary objective is to pivot to areas that our clients are focusing on, such as digitalization, ESG, and supply chain management.

**With a change in government administration, how has the regulatory landscape evolved?**
The life sciences industry is keeping its eye on H.R.5376, a legislation related to drug pricing that will require producers and pharma companies to behave differently. This regulation as part of the Build Back Better Act will require our clients to double down on value-based contracting and outcomes-based pricing. They will not only assign a price to a pharmaceutical product but will also commit to an outcome for which they can charge differently.

There is attention on how the Federal Trade Commission (FTC) in the US will regulate M&A activity. With a focus on protecting the public against anti-competitive behavior and unfair trade practices, the FTC can require a merging company to divest assets and rights to refrain the new company from having a monopoly position in the market.

Additionally, the FDA has implemented a draft reporting program so that certain key quality metrics are reported to the agency in an effort to ensure continual improvement of product and process quality in the pharmaceutical manufacturing industry. Given the complexity of pharmaceutical businesses, the supply chain cannot afford one misstep, and consequently the product and process quality have become even more important.

**Our primary objective is to pivot to areas that our clients are focusing on, such as digitalization, ESG, and supply chain management.**

# Arda Ural

Partner & EY Americas Industry Markets Leader,
Health Sciences and Wellness
**EY US**

**How has the Omicron wave altered the IPO and special purpose acquisition company (SPAC) landscape, and what is the trajectory we can expect to see in 2022?**
IPOs in 2021 were at an all-time high, but factors causing uncertainty such as potentially increased interest rates, geopolitical tensions, inflation risks, and the possible emergence of new Covid-19 variants, may hinder economic recovery and play a role in the financing environment in 2022.

IPO candidates should remain flexible with a plan B in place to meet financing needs in case the IPO timetable is delayed. SPACs are currently in a more dire state than in 2021 due to the decreased availability of late-stage assets and the window for IPOs starting to close. Companies need to start prioritizing their pipelines to put their next milestone in sight and avoid dilution. I believe that companies without a current late-stage asset will experience choppy waters in this uncertain environment.

**Related to the topic of an aging population, what innovations are entering the market?**
Population age continues to feed what diseases pharmaceutical companies need to target, and oncology is by far the most common disease area of focus for pharma. In addition to oncology, cell and gene therapies are starting to receive significant focus as a way to address patient and population needs.

**Which of EY's services are in most demand within the life sciences sector?**
EY continues to focus on addressing business challenges enabled by technology-inspired solutions, and especially today, digitalization is extremely important to our clients. ESG has also become a massive trend that is here to stay as investors and stakeholders want better ESG disclosures to help them understand more about how a company performs. Consumers also want to understand the impact their choices are having on the world, and employees seek to know whether their company is driving greater equality, empowerment, better working conditions and safer and more sustainable communities. EY assists our clients in their ESG goals through nonfinancial reporting advisory and assurance, climate-related reporting, sustainability and supply chain advisory, and outcomes measurement. ■

# The Life Sciences Investment Climate

## A reckoning?

During the period of Covid-related anxiety in which the industry received unprecedented media coverage, governments pitched extensive resources into combatting the spread of the virus. The ensuing 'lockdowns' meant that people had more time at home, and more time therefore to spend on online trading platforms, and much attention was drawn towards biotech. Zero interest rates also helped ensure that huge amounts of capital flowed into high-risk technology. Furthermore, according to Pitchbook data, venture capital firms invested record amounts of capital in the biotech industry over the past two years – US$12.6 billion in 2020 and US$16.1 billion in 2021. Overall, IPOs pulled in almost three times more than in previous years. Over half of these were for preclinical or phase 1 companies.

The frenzy has now ended, however, and the pendulum has swung far – arguably too far, according to some observers – in the other direction. In early 2022 the Financial Times reported that 83% of recently listed US biotech and pharma stocks were trading below their IPO price in what they called a "stock market bloodbath." Yet there is a Wall Street adage that in a strong wind even turkeys can fly, meaning that in a booming market it is nearly impossible to distinguish the winners from the losers.

Christiana Bardon, co-managing partner of MPM's BioImpact Capital and portfolio manager of BioImpact Equities and Oncology Impact Funds, believes this period of dramatic correction is currently close to the bottom, given that many biotech companies are trading at cash balances. From Bardon's perspective, the extreme market corrections have been largely appropriate. "Many of these corrections are appropriate, because a lot of credit was given to companies that had exciting technologies or platforms but were still far from developing a real drug that would enter a clinical trial, receive regulatory approval, and ultimately help patients," said Bardon. "Not all companies deserve to have their assets taken forward. Having a more stringent funding environment is not negative; it just means that companies must generate clinically meaningful data to deserve their valuations."

Chris Garabedian, chairman and CEO of the life sciences accelerator Xontogeny, views the market corrections from a similar perspective. "After record years of private investment, facilitating crossover rounds and taking companies through IPOs, people are realizing that our sector may need to be more discerning in deciding which companies are worthy and mature enough to bring to the public markets," said Garabedian. "Tough times can scare off newer investors and entrepreneurs, which is not all bad. These cycles help to screen out those investors and entrepreneurs who are not as committed to creating and reaching a long-term goal."

While it may appear that companies with good technology are being indiscriminately punished just as they had been indiscriminately rewarded earlier in the pandemic, the shift has been an important one in remembering the fundamentals of the industry: no matter how sexy a particular company's technology or platform is, the end goal must remain to provide products that help patients live healthier, longer lives.







**More M&A activity?**

What remains uncertain is the extent to which the cooling down of the market will trigger increased M&A activity. Some believe that large pharmaceutical companies like Pfizer and Merck that had been observing over-valuations from the sidelines may find the current climate more suitable for action.

EisnerAmper, one of the largest accounting, tax and business advisory firms in the US, helps life sciences companies going through IPO or secondary offerings. John Pennett, partner-in-charge of the national technology and life sciences group, revealed that the company is increasingly busy with new company formations, with four clients going public in Q4 of 2021 alone. While this is in many ways a testament to the perennial dynamism of the industry, it does not serve as a litmus test for the current state of the life sciences financial climate.

According to Lori Hu, managing director of Vertex Ventures HC, the industry is currently experiencing a temporary "hangover" effect and the market will soon bounce back. "Expectations to finance for the long term are again receiving priority," explained Hu. "The M&A market has been relatively slow over the past year, as pharma executives wait on the sidelines for the valuation correction to play out, but I believe that we will see M&A activities increase in this coming year."

> Tough times can scare off newer investors and entrepreneurs, which is not all bad. These cycles help to screen out those investors and entrepreneurs who are not as committed to creating and reaching a long-term goal.
>
> **– Chris Garabedian, Chairman and CEO, Xontogeny**

For others, this shift may not happen quite so definitively. James Gale, founding partner and managing director of Signet Healthcare Partners, commented: "As the capital market valuations fall back and exits via the public markets become less viable or attractive, sellers may pause. At the same time, buyers may be affected by rising interest rates and the change in the market to dig in on lower pricing. We could thus see a protracted period of lessened activity before we see the M&A markets start to build again."

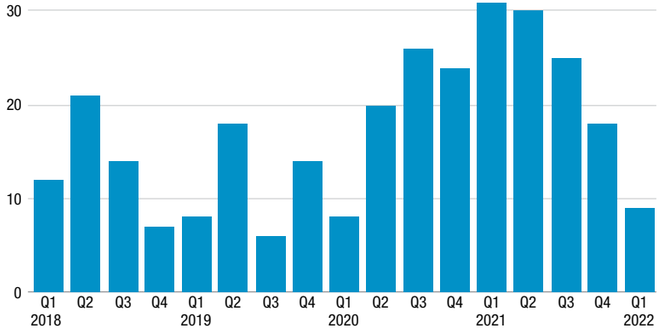
The conviction that lower valuations will lead to more M&A activity is not shared by all industry stakeholders. MPM Capital's Bardon believes the level of activity will remain consistent despite the market turbulence, as pharmaceutical companies are constantly on the hunt for new and innovative drugs to incorporate into their distribution pipelines after undertaking thorough due diligence. "M&A is like picking apples – you only want to eat the apple when it is ripe. No one wants to eat an unripe apple, even if its 50% off. Similarly, M&A occurs when companies meet their proof of concepts and have de-risked their assets such that the drug looks promising to be successful in future clinical trials," said Bardon. "The question that remains is which companies are ripe and ready for the picking."

Overall, the health of the life sciences investment climate is expected to return to the trajectory it had been on pre-pandemic. "We are excited about the health and the growth of the industry and the pace at which it has continued to evolve over the last 20 years," commented Ryan Meany, managing partner of Edgewater Capital Partners. "The hallmark for us is its malleability to consumer needs, which has manifested in important therapies and broad adaptability to the business model and cycle."

The past two years have brought about unprecedented levels of interest and investment and reshaped the way the broader world interacts with life sciences companies, particularly in biotech, and this bodes well for the financial support it will attract in the years to come. ■

**After setting record pace, biotech IPOs slump to start 2022**

Number of biotech IPOs priced, by quarter




Source: BioPharma Dive

**What is your assessment of the current health of the life sciences investment climate?**

Since the peak of capital inflow into the industry in February 2021, we have been in a period of dramatic correction where the biotech indices have fallen over 50%. I believe we are close to the bottom of that correction period because many biotech companies are trading at cash balances, meaning very little is being attributed to their technology and programs.

Many of these corrections are appropriate, because a lot of credit was given to companies that had exciting technologies or platforms but were still far from developing a real drug that would enter a clinical trial, receive regulatory approval, and ultimately help patients. When shifts like this happen, we must remember the fundamentals of the industry; despite how attractive a company's technology or platform may be, the ultimate goal is to make progress towards bringing new drugs to patients.

Additionally, not all companies deserve to have their assets taken forward. Having a more stringent funding environment is not negative; it just means that companies must generate clinically meaningful data to deserve their valuations. I see corrections as a positive force in the industry, as it reminds us of basic principles such as capital efficiency.

MPM Capital is optimistic about the future and sees the present as a great buying time to be entering the market. The long term fundamentals on the industry are healthy and intact.

**Do you believe this market correction will lead to an uptick in M&A activity?**

I do not believe that lower valuations lead to more M&A activity. M&A is like picking apples – you only want to eat the apple when it is ripe. No one wants to eat an unripe apple, even if its 50% off. M&A occurs when companies meet their proof of concepts and have de-risked their assets such that the drug looks promising to be successful in future clinical trials. From this perspective, the M&A environment is evergreen, which is that pharmaceutical companies have an ongoing need for new and innovative drugs to fill their commercial distribution pipelines and they want to buy companies who have met their proof of concept.

> **Having a more stringent funding environment is not negative; it just means that companies must generate clinically meaningful data to deserve the valuations they are fundraising at.**

# Christiana Bardon

Co-Managing Partner, MPM's BioImpact Capital and Portfolio Manager, BioImpact Equities and Oncology Impact Funds
**BIOIMPACT CAPITAL LLC, AN MPM COMPANY**

**To what extent has the turbulence impacted MPM Capital's portfolio companies?**

MPM Capital portfolio companies were the beneficiaries of a great capital fundraising environment over the past two years. Many of our portfolio companies had the opportunity to raise private financing, IPO and secondary financings as public companies. That said, all our companies have been affected by both the upward and downward drafts, but we hope they will go on to be successful in their clinical trials. At the end of the day, a successful outcome is how you create value, and it is not subject to volatility.

**What advancements within the biotech industry are you most excited about?**

In the oncology space we are in the middle of an incredible period of innovation, particularly regarding the genome sequencing revolution. This started in the early 2000s when we sequenced the first human genome. Two decades later, we now have genetic information about almost every cancer patient as well as about various rare diseases. We can start to understand the genetic causes of diseases and therefore what targets we should address with our new developed drugs. Additionally, we have developed many genetic tools that have enabled whole new classes of treatments, such as using living cells and living viruses to treat cancer or genetic illness. We are in the midst of an incredible innovation era that is only accelerating. For example, last year we saw the first patient who was genome edited and cured of their hereditary genetic disease.

Several innovations abound regarding RNA and DNA; mRNA enabled us to vaccine the world against Covid-19. Circular RNA is particularly exciting as it enables us to not only deliver RNA more broadly to the organs but also to produce proteins beyond for vaccination purposes.

**Looking ahead, what themes will MPM Capital hone its investment around?**

We are on our second oncology impact fund. While we have made great progress regarding immunotherapy, cell therapies, and our ability to cure certain types of cancers, we cannot yet cure all patients with those cancers, nor can we cure all cancers. We still see a lot of exciting work to do in this space. Additionally, we are excited about the next frontiers in virology and neurology. ■





**What have been the key milestones for Signet over the past year, particularly with the company's Fourth Fund (Fund IV)?**

Signet has made several investments in Fund IV. We completed the investment in Ascendia Pharmaceuticals in the first half of 2021. We participated with Novo Holdings in acquiring Altasciences, a fast-growing, well-run clinical research services organization. We also made a strategic investment into Juno Pharmaceuticals, a Canadian marketer of complex generic injectables. Signet is hoping to leverage relationships with our portfolio companies and other entities to find products for investment and to create partnership arrangements. In early 2022, we acquired the consumer health contract manufacturing business of Fagron, a Dutch personalized medicine pharmaceutical company. This acquisition was done not through Fund IV, but rather through a special investment vehicle and fits in with Signet's theme of investing in consumer health.

**To what extent do you see the general correction of market activity as an opportunity for the industry?**

Signet's thesis is that interest rates will rise. Rising interest rates will have an effect in two parts. First, there is generally a rotation in the investment market away from high-tech growth and futuristic earning streams towards companies with revenues and earnings today. The decline in public share prices of biotech companies over the past six months reflects that pivot towards value. Second, if interest rates climb, the cost of capital climbs. This has a converse effect on multiples – meaning multiples come down as the cost of capital rises. If this happens, perceptions of valuation begin to shift on the buy and sell side. However, multiples often slowly decline, which induces a period of disintermediation between buyers (who sense it has become a buyers' market and offer lower prices), and sellers (who still have a memory of higher valuations and hold their ground). It is then difficult to bridge the gap between bid and ask unless people are becoming more financially desperate to sell. We could thus see a protracted period of lessened activity before we see the M&A markets start to build again.

> **We see a risk of rationing of capital by biopharma companies leading to a pullback in the amount of funds being spent in R&D.**

# James Gale

Founding Partner & Managing Director
**SIGNET HEALTHCARE PARTNERS**

**How have these trends impacted Signet?**

We build our investment models around particular investment situations, paying careful attention to terminal values and exit multiples. We assess the climate relative to historical norms under different interest rate environments. Additionally, as we build an investment case, we are often risk adjusting management's robust projections to consider downside scenarios. This includes the prospect of a delay in the recovery of financing for biotech companies. We see a risk of rationing of capital by biopharma companies leading to a pullback in the amount of funds being spent in R&D. We are cautious with our portfolio companies about rapid increases in personnel or capital expenditures in capacity until we have better visibility about the future utilization of that capacity. We thus have a wary eye about the impact of a slowdown in biotech financing on R&D spend and CDMO profitability.

**How do you view the feasibility of reshoring efforts for American manufacturing of pharmaceuticals?**

India's actions recently have raised questions about the security of drug supply from that country, traditionally a reliable partner. At the start of 2020, they temporarily placed an export ban on 27 critical medications and in 2021, redirected Serum Institute to reprioritize the production of the AstraZeneca vaccine for their domestic market. More recently, India's tilt towards Russia in the Ukraine-Russia war further raises questions about their alignment of interest with the US.

We clearly need to secure drug supply in the US. That said, the market structure in the US, particularly for the purchase of generic medications which account for 80-85% of all prescriptions, disincentivizes onshoring of production. While branded pharmaceutical companies would prefer to keep production closer to the markets they serve to mitigate potential supply chain disruptions, the generic industry is still highly dependent on India and China.

**What key trends do you see driving growth for Signet over the next few years?**

Signet's investment strategy is guided by determining which technologies will be potential winners. We also track complimentary services that can create a more comprehensive offering to customers. While Signet is a commercial stage growth equity fund, technology guides our investment decisions.■

> The past 12 months have been busy as we have seen a significant amount of new company formations, which require accounting, tax advisory and structuring support.

# John Pennett

Partner-in-Charge of the National Technology and Life Sciences Group
**EISNERAMPER**

**Can you give an overview of EisnerAmper's activities and performance in the life sciences sector over the past year?**
The life sciences division is the leading industry vertical for our public company practice, more specifically for companies that are going through IPO or secondary offerings. The past 12 months have been busy as we have seen a significant amount of new company formations, which require accounting, tax advisory and structuring support. We have also seen many companies going through significant M&A transactions and/or preparing for IPOs. In Q4 of 2021 alone, we had four clients go public, which was extremely exciting. The largest growth engine for us is the capital markets, and if they stay strong, it will be greatly beneficial to our business moving forward.

EisnerAmper has added capabilities to its portfolio, including grant accounting capabilities in our South Florida office; managed services, which allow virtual companies to have a managed services computer solution; and outsourced accounting capabilities in San Francisco through acquiring Keating Consulting Group, which provides outsourced financing and accounting services to venture-backed companies. We continue to increase our geographical footprint.

We aim to become more visible and reach all the life sciences communities in the areas where we operate. We support universities and their entrepreneurial programs, and regularly speak at various events, accelerators and incubators, encouraging entrepreneurship.

**How many entrepreneurs have you seen successfully form companies and IPOs?**
Across the technology and life sciences community, we have seen many entrepreneurs become successful. They mostly gain their experience in larger organizations, and from there start their own companies from the experience and lessons learned. From a public company perspective, credibility is critical, and we are seeing this even more so in the venture capital community. At the early stage of investment, if you are not able to secure a significant venture capital round it will be very difficult to do so at a later stage. If you do not have the inside track from the beginning, it is hard to get there as there is a significant volume of companies with interesting ideas, and investors are going to the sources they feel are most likely to succeed.

**What advice would you give first time entrepreneurs?**
Finding a strong partner to help supplement skill sets is extremely important. For example, if it is a scientific founder, finding a partner with business development expertise can be critical. At a very early stage, companies do not necessarily have the funds to bring such a person on board, but we have seen creative deals where the company is able to share some equity, most often a future equity arrangement and maybe a promise of employment when the company is funded. There are also public and private incubator groups that help early-stage companies complete their management teams and skill sets by using an outsource model.

**What can we expect to see in the M&A and IPO landscape moving forward?**
The IPO markets have certainly tightened with a bit of a slowdown in the process. There is still a substantial amount of money to be spent, some deals are still getting done, and a lot of companies are in the queue to go into the public marketplace. There has been pressure on biotech stock, and some of the recent vintage biotech IPOs are trading well below their IPO price. This is not a great sign for the industry as a whole, but there is still cautious optimism for what the markets are going to look like for at least the first part of 2022.

**If there was one thing you could change in the Tax Act that would help people across the board, what would it be?**
An expansion of the R&D credit, which will help innovative companies attract more capital to allow them to determine if their science is worthwhile.

**Which services have been in most demand and driving growth for EisnerAmper?**
Support for IPOs and SPACs—whether they be tax, auditing or consulting clients—has been in significant demand. EisnerAmper has seen substantial growth in its tax services division, with demand coming especially from clients that have an international aspect to their businesses. We are also supporting companies regarding ownership and the tax ramifications surrounding shares and stock options, especially as companies are growing and thinking about what an exit might look like. ■





# Chris Garabedian

Chairman and CEO
**XONTOGENY**

**How has the biotech sector been impacted over the past year and how did Xontogeny's activities evolve?**
The past year saw significant pull-back in public valuations. The XBI had one of its worst years on record in 2021, which continued into 2022. After record years of private investment, facilitating crossover rounds and taking companies through IPOs, people are realizing that our sector may need to be more discerning in deciding which companies are worthy and mature enough to bring to the public markets.

We set out with an early private equity model that would work in any macro-market environment. We developed our thesis around investing in lead products that focus on specific value creation.

**Can you highlight some upcoming investments Xontogeny is excited about?**
We are continuing to incubate companies at Xontogeny and anticipate announcing several new seed investments in this upcoming year. We are very excited when these companies receive their Series A funding, often through the Perceptive Xontogeny Venture (PXV) fund, created through a strategic relationship between Xontogeny and Perceptive Advisors. Between our funding mechanisms for Seed and Series A investments, we have a full portfolio of over 20 companies.

**How do you see Xontogeny evolving?**
We want to create the next generation of biotech leaders not only through financial investment, but also through exposing them to the decades of experience of our team. ■

# Lori Hu

Managing Director
**VERTEX VENTURES HC**

**How does Vertex differentiate itself in the market?**
Vertex is a global investment fund with offices in the US, China, Singapore, India and Israel. Vertex is a female-led fund, and we strive to increase diversity. We are driven by early stage science and are pragmatists in the way we deploy capital to most effectively drive companies to success.

**What have been the recent highlights?**
Over the past year we invested in Sonoma Biotherapeutics, which uses a Treg therapy platform to treat autoimmune diseases; Allay Therapeutics, which delivers durable pain relief in an effort to reduce the opioid usage in the US; and Indapta Therapeutics, which has developed a natural killer (NK) cell therapy platform to increase access to cell therapies for cancer patients.

**What is Vertex's vision for 2022 and beyond?**
We want to develop products that can deliver a step-change benefit for patients. The market will always have ups and downs, but we remain optimistic about funding new science and innovation. We are always excited to invest in and partner with new companies working towards making a difference for patients worldwide. ■

# Ryan Meany

Managing Partner
**EDGEWATER CAPITAL PARTNERS**

**What excites you about the life sciences space?**
We are excited about life sciences because of the development opportunities for small to middle market enterprises outside the control of big pharma. This is due to the increased development of personalized medicine, particularly with the advent of gene therapies.

We are also observing a shift away from one-size-fits-all drugs, which creates more opportunities for CDMOs and CROs—spurring the development of mid to small biopharma companies that match our portfolio. Finally, the speed of recent innovation in the life sciences has been profound, as exemplified by the Covid-19 vaccine rollout, which bodes well from a growth standpoint.

**Could you speak to the consolidation trend in the CDMO industry and the attractiveness of CDMOs from a private equity standpoint?**
While we have only invested in hybrid CDMOs in the past, they are attractive to private equity in the sense that they combine traditional manufacturing with cutting edge technology.

We are bullish on CDMOs because of several domestic trends, including a general onshoring effort that is being driven largely by quality control concerns from pharma. ■

# The Life Sciences Regulatory Climate

## Clearing up confusion about quality metrics

Image courtesy of Mammoth Biosciences.

In 2015, the FDA produced an original draft of an initiative to create a more objective system of measuring, evaluating, and monitoring both the product and process lifecycle within pharmaceutical manufacturing. Seven years and a few revisions later, confusion remains over exactly how companies should incorporate the FDA Quality Metrics report to measure quality management. The most basic problem deals with the obfuscation of the metrics themselves.

"When it comes to quality metrics there remains no consensus on definitions – for example what constitutes a 'batch'?" posited Gil Roth, president of the Pharma & Biopharma Outsourcing Association (PBOA), a non-profit that works to enhance the regulatory and legislative business interests of CDMOs. "My standard joke for this is that until we all spell 'harmonization' the same way, we are not going to make a lot of progress. We need to have a common language."

The result of this confusion is that even companies that want to comply have difficulty understanding how to. Furthermore, the report's industry-wide implementation may actually cause more harm than good in terms of operations.

For CMOs and CDMOs that make an expansive range of products, one small slip-up may not be representative of overall operations. For facilities that handle only one product, any problems could ruin the entire operation's reputation. Roth sees a reputational problem at play: "The FDA has been pushing to create a rating system for all sites, so payers can pressure license holders into revealing their manufacture site ratings. This involves public shaming and splits the goal of what Quality Management Maturity Metrics are supposed to do: incentivizing quality vs. identifying potential quality problems that could lead to shortages. These are issues for the whole value chain, not just CMOs."

To their credit, the FDA acknowledges that reception of its Quality Metrics could be more positive and has requested feedback from industry stakeholders. In March 2022, the administration established a docket to solicit comments on changes to the reporting program and will accept recommendations until June 7, 2022. Despite its complications, the Quality Metrics Reporting program remains imperative, especially with the heightened sophistication of manufacturing.

Arda Ural, partner and EY Americas industry markets leader health sciences and wellness, acknowledged: "Given the complexity of pharmaceutical businesses – with focus now shifting to biologics, antibodies, and cell and gene therapies—the supply chain cannot afford one misstep, and consequently the product and process quality have become even more important."

Rather than simply discard the initiative, the administration should continue to collaborate meaningfully with those it affects most directly. The current minimum standard to ensure a manufacturer's products are of safe and sufficient quality is through compliance with CGMP requirements. Yet CGMP compliance by itself does little to demonstrate whether that company is actively striving to improve its sustainable compliance. Quality metrics can help evaluate supply chain robustness by demonstrating opportunities to improve manufacturing practices. As such, decision makers at contract manufacturing companies would be wise to offer their feedback within the FDA's designated timeframe to ensure their voices are taken into account concerning future renditions of the initiative.

### Drug pricing remains contentious

The issue of drug pricing in the US has always been messy, and the failure to address the issue at the federal level has further complicated matters. As a result, state governments are attempting to independently regulate their jurisdictions. Over the past year, roughly 500 drug pricing bills were introduced by state legislators with the aim of forcing drug price transparency, capping price increases for state payers, and regulating PBMs. For example, West Virginia recently passed a law mandating that rebates and discounts currently offered by biopharmaceutical companies to insurers and other intermediaries will be shared with patients. In 2020, the state's legislature had passed a bill requiring pharmaceutical drug manufacturers and companies offering health benefit plans to submit pricing information to be posted on the state transparency website.

Anne Pritchett, senior vice president of policy, research and membership at PhRMA, a trade group that lobbies on behalf of pharmaceutical companies, believes such reforms can be beneficial. Speaking on behalf of her organization about its patient-centered agenda, Pritchett said: "There is no doubt that the system needs to work better for patients, and many common-sense reforms are available to policymakers who support helping patients access and afford the medicines they need… We support policies to address market distortions such as 340B reforms and policies like the West Virginia law that requires the rebates and discounts that insurance companies and middlemen receive are shared directly with patients at the pharmacy."

For Pritchett, such reforms are clear ways to address issues like the high out-of-pocket costs patients see due to the increasing use of deductibles and coinsurance. Yet according to Jason Parish, co-leader of the life sciences industry group at Buchanan Ingersoll & Rooney PC, the consequences of state-level involvement do not mirror these legislators' intentions: "The result is a complicated patchwork of regulation around the country, and one of the perverse side effects of this is that creating transparency in the system has led to higher prices. The problem of not having federal legislation in place is far bigger than anyone recognizes and has gotten worse throughout the pandemic."

In addition to leading to purportedly higher prices, many worry that the current regulatory environment is threatening the very ethos of the life sciences industry – its cult of innovation. Speaking of the current policy environment under the Biden administration, Donna LaVoie, president and CEO of LaVoieHealthScience, acknowledged that no real progress has been made on the problem: "The regulation of drug pricing remains an ongoing issue, with many drugs treating rare diseases retailing at prohibitive prices. The trade-off of innovation and drug pricing is a tricky topic and not one that has been resolved."

James Sapirstein, chairman, president and CEO of First Wave BioPharma, believes that what the general public typically fails to understand about the high price tags associated with the industry is that US companies have a narrow window to monetize their product under patent before restrictions are lifted and generic companies enter the marketplace with alternative formulations. The money gained during this initial period is crucial for gaining capital for new developments. "Although I believe that we should do whatever we can to provide access to drugs for patients that need medications, patenting is very important," explained Sapirstein. "If a company cannot protect its rights and have the ability to make some kind of money on what it's developing, there will never be innovation."

This is a top concern not only for pharma companies but also for certain CDMOs that deal with complex manufacturing processes such as technologies related to drug device combination or complex nanoparticles. While these types of technologies pave the way for future innovative therapeutics that may ultimately help patients, their sophistication impacts the cost of manufacture and thus the cost of goods. "I am concerned the current regulatory environment will make innovation more challenging as it will become increasingly difficult to justify the costs of certain products," admitted Robert Lee, president of the CDMO division of Lubrizol Life Science, which, for this reason, sticks to technologies he views as scalable and cost-effective.

Some drug manufacturers have found alternative ways to bring their products to market to lower costs. When Medicure Inc. went to introduce its cardiovascular drug Zypitamag to the market, the company found it challenging to attain insurance coverage given the low pricing of generics. Not wanting to increase the price of the drug in accordance with the desires of PBMs, Medicure Inc. decided instead to sell directly to people who are uninsured or underinsured through a partnership with North Carolina-based pharmacy Marley Drug. "Through our partnership with Marley Drug, we sell Zypitamag for just US$1/day and are generating more revenue than if we had insured the product through a PBM," commented Albert Friesen, the company's CEO and chairman of the board. "In truth, most pharmaceuticals are inexpensive to make, and it is the insurance that significantly drives up costs."

With no clear-cut solution, the problem of drug pricing continues to fester unproductively. The elusive challenge is to find a compromise that allows for an innovative research, development, and manufacturing climate while ensuring patients can afford the medications they need. Looking beyond the cost of innovation, legislators should also pay attention to the earnings made by intermediaries downstream. ■

> Through our partnership with Marley Drug, we sell Zypitamag for just US$1/day and are generating more revenue than if we had insured the product through a PBM. In truth, most pharmaceuticals are inexpensive to make, and it is the insurance that significantly drives up costs.
>
> **– Albert Friesen, CEO & Chairman of the Board, Medicure Inc**

# Anne Pritchett

Senior Vice President of Policy, Research and Membership
**PhRMA**

**Could you introduce our readers to PhRMA?**
PhRMA represents the nation's leading biopharmaceutical research companies. Our organization advocates for public policies that encourage the research and development and manufacturing of new medicines that allow patients to lead longer, healthier, and more productive lives.
We are also engaging with policymakers and others on health care reforms to make life-saving medicines available and affordable for patients and to support more equitable health care delivery.

**What role can state and federal legislatures play in establishing more accessible drug pricing?**
There is no doubt that the system needs to work better for patients, and many common-sense reforms are available to policymakers.
PhRMA works with policymakers across the country, focusing on policy solutions that address issues like the high out-of-pocket costs patients see due to the increasing use of deductibles and coinsurance. West Virginia, for example, has passed a law that ensures rebates and discounts already given to insurers and other middlemen by biopharmaceutical companies are consistently shared with patients to lower costs at the pharmacy counter. Similar legislation is under consideration in other states.
At the federal level, we are advocating for ideas that would modernize the Medicare Part D prescription drug program by capping what seniors must pay each year for medicines, lowering cost sharing and making seniors' costs more predictable each month.

**How can the industry at large enhance its global supply chains to increase efficiency and resiliency?**
We support policies to further enhance resiliency in our supply chains, such as policies to support on-demand manufacturing, adoption of the regulatory flexibilities implemented during the pandemic to allow manufacturers to quickly respond to emerging threats, and federal investments to address critical infrastructure gaps such as the significant gaps in the STEM workforce, all of which are needed to fuel continued innovation. ■

# Gil Roth

President
**PHARMA & BIOPHARMA OUTSOURCING ASSOCIATION (PBOA)**

**Which are the most important initiatives the PBOA has been involved in over the past year?**
Negotiating the third iteration of the Generic Drug User Fee Amendments (GDUFA) between the FDA and industry, which happens every five years, was key. We also focused on pandemic response and preparedness—how our members are helping license holders and governments stock up and produce vaccines and therapeutics for Covid-19, figuring out next steps, and how the supply chain will respond. This has involved on-shoring discussions, given the last two administrations have pushed to manufacture more domestically.

**How has the pharma and biopharma landscape evolved with the Biden administration?**
The current administration has been employing the Defense Production Act (DPA), an industrial policy where the government is able to give suppliers rated orders—if a Covid-19-vaccine manufacturer is in need, suppliers must sell to them before selling to non-vaccine manufacturers in the sector. This has led to ensuring adequate supplies of vaccines but could cause shortfalls throughout the supply chain for components needed by other manufacturers. We have worked with the new administration to highlight potential challenges and solutions on this, especially on the biologic side. PBOA wants to ensure that the DPA is used more judiciously so the supply chain can ultimately achieve equilibrium again.

**Is FDA making progress on Quality Metrics?**
Our concern with quality metrics has been the potential for inherent bias against CMO facilities, because of the sheer quantity and breadth of products that many of our members make. The FDA have been pushing to create a rating system for all sites so payers can pressure license holders into revealing their manufacturing site ratings. This involves public shaming, and splits the goal of what Quality Management Maturity Metrics are supposed to do: incentivizing quality vs. identifying potential quality problems that could lead to shortages. There are issues for the whole value chain, not just CMOs. ■





# Donna LaVoie

President & CEO
**LAVOIEHEALTHSCIENCE**

**Could you describe your client profile?**
LaVoieHealthScience has three kinds of clients: first, there are companies that are launching out of venture, led by entrepreneurs or sophisticated executives from large pharma. Second, we work with small to mid-cap companies. Lastly, we have larger-cap and commercial-stage clients. While their needs may differ, the connective link is strategic communication. All of these companies are tasked with telling a story beyond the science. Our job is to make their companies' technologies and products more understandable and increase awareness.
An important industry trend is the importance of strategic communication for all stakeholders. The surge of communication need has increased exponentially as companies recognize the necessity of conveying a differentiated story amid the unprecedented number of financings and IPOs over the last two years.

**How has the policy environment under the Biden administration impacted the life sciences landscape?**
The regulation of drug pricing remains an ongoing issue, with many drugs treating rare diseases retailing at prohibitive prices. The trade-off of innovation and drug pricing is a tricky topic. A bigger issue is the FDA's contradictory stance on accelerated approvals of innovative therapies and the impact the FDA has on clinical progress and approvals, which induces uncertainty in the markets.

**What do you hope to accomplish by 2023?**
We intend to sustain the expansion of our service offerings in our active areas. This is evidenced by the increase in our media relations, social media and public market ambassador capabilities.
Looking into the future, LaVoieHealthScience has longer-term interests in expanding its geographical footprint. We recently expanded into the Midwest, which provided an opportunity to source great talent with its beltway of pharma and biotech companies and several key professional associations. We aim to develop a hub of a people in strategic markets. ■


# Edward Allera & Jason Parish

Co-Leaders — Life Sciences Industry Group
**BUCHANAN INGERSOLL & ROONEY PC**

**What types of counsel have clients been coming to Buchanan Ingersoll & Rooney PC (Buchanan) for?**
**JP:** In the early 2010s, I saw a lot of product liability and drug pricing issues within the litigation context. I have seen a shift regarding the latter from more opportunistic private plaintiffs to government entities at the state and federal levels bringing litigation against pharmaceutical companies, typically under antitrust and consumer protection statues. Additionally, the administration shift has brought on a few changes. Under Trump, there was a framework for addressing drug pricing issues that the Biden administration has taken up a notch.
**EA:** We will see a dramatic uptick in compliance activities as authorities start to take action that has been delayed due to Covid-19.

**How can innovation and technology effect drug pricing?**
**EA:** Innovation remains critical – 90% of units sold are generics with prices on the floor. The question becomes how to convert your sunken cost into a value-add, and the answer is technology. While people focus on getting FDA approval, investors also want to know how their investment will generate returns. Buchanan has been spending time with clients to understand how payers function, how clinical trials can be decentralized to reduce overall costs, and ultimately how to get something of value to the market.
**JP:** The failure to address drug pricing at the federal level has led to interesting developments. Many states are trying to independently regulate, as demonstrated by the approximately 500 drug pricing bills introduced by state legislators over the past year, a handful of which have been enacted. These states are looking to force drug price transparency, cap price increases for the state payers, and regulate PBMs. The result is a complicated patchwork of regulation around the country, and one of the perverse side effects of this is that creating transparency in the system has led to higher prices. ■

# INTRODUCING THE HUBS

"To be a successful hub for bio innovation, a region must have strong biological and physical sciences, engineering, medical schools and academic hospitals, and biotech and pharma companies. There are two epicenters with that kind of confluence, Boston and San Francisco, and these regions lead the biotech industry on a national and perhaps global level."

**– David Schaffer,**
**Director,**
**QB3-Berkeley**



Image courtesy of Syngene

# Massachusetts

Source: MassBio

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**

**BOSTON**
**CAMBRIDGE**
**CORE**

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

**NIH funding US$3.711 billion,
35.2 million square feet,
(according to CBRE)**

**WORCESTER**

**WEST**

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

**128/SUBURBS**

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

**SOUTHCOAST**

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

**#1**
**REGION**
**for NIH Funding**





# New Jersey

Source: Choose New Jersey

Quest Diagnostics
Catalent
Allergan
Quintiles
Stryker Orthopaedics
Ferring
BD
Bayer Healthcare
GlaxoSmithKline
AbbVie
Daiichi Sankyo
Parexel
Frontage Laboratories
Cambrex Corporation
Pfizer
Pfizer
Novartis
GlaxoSmithKline
Valeant
Biotrial
Zoetis
Merck
Celgene
Janssen
Daiichi Sankyo
Amneal
Eli Lilly
Roche
Insmed
PTC Therapeutics
Catalent
Pfizer
Allergan
Novo Nordisk
Bristol-Myers Squibb
Dr. Reddy's Laboratories
Johnson & Johnson
Sandoz
Covance
Parexel
Bristol-Myers Squibb
Otsuka
Aurobindo
Janssen
PPD

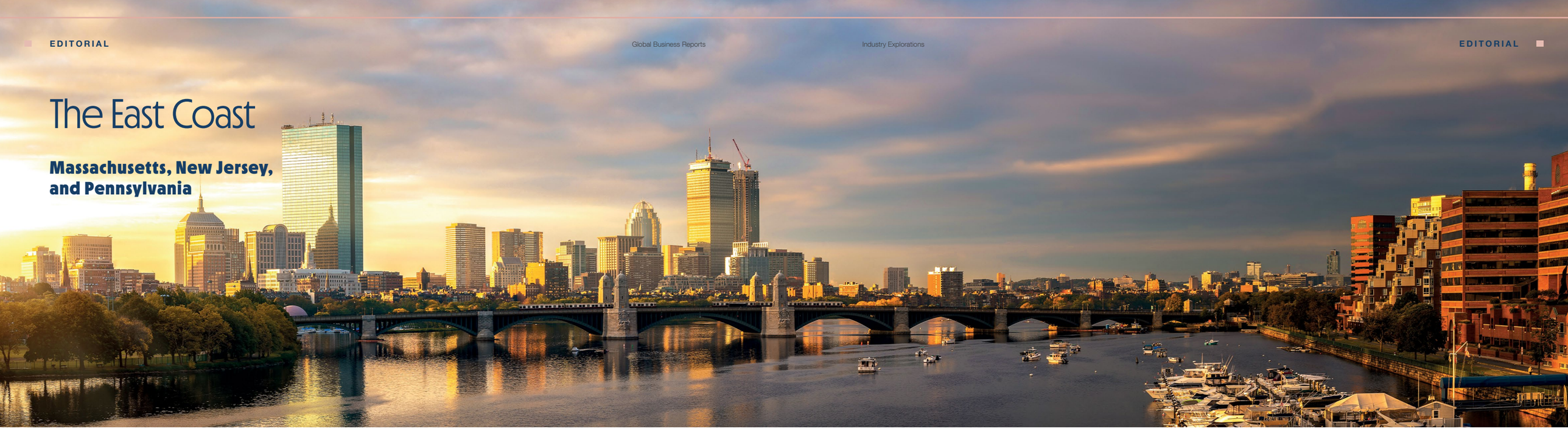
**PHARMACEUTICAL
AND BIOTECH CLUSTERS**

**#2**
**REGION**
**for NIH Funding**

EDITORIAL

# The East Coast

## Massachusetts, New Jersey, and Pennsylvania



A trip down the East coast is in many ways a history of the birth of an industry. Start from the cobblestoned streets that wind through Boston, where George Washington decided to begin building naval warships in the late eighteenth century, laying the groundwork for the city to become a manufacturing hub for centuries to come, head south towards New Jersey, New York, and Pennsylvania, where innovation is carved into the regional blueprint, home to the first hospital and medical schools in the country, until you reach North Carolina, where its Research Triangle region has become a magnet for people seeking employment in the life sciences. The East Coast has long been at the forefront of the global life sciences industry.

### Massachusetts

Massachusetts, home to the powerhouses of Boston and Cambridge, repeatedly ranks among the top places in the world for life sciences innovation. In addition to playing an outsized role in the industry, the industry itself plays a large part in the overall ecosystem of the state. Hospital systems, nursing facilities, and residential care are the largest contributors to the state's GDP.

Massachusetts receives immense venture capital funding, second only to California. This funding is particularly directed towards the health technology space; Massachusetts is home to approximately 500 medical device manufacturing companies that collectively employ nearly 25,000 people. It is an ecosystem home to some of the biggest international players, such as Thermo Fisher Scientific, which draws in approximately US$40 billion in annual revenues and has over 90,000 global employees – but also home to some of the most innovative young startups in the country. The energy is palpable.

"2021 was a very exciting year for the Massachusetts life sciences ecosystem with US$13.6 billion dollars of venture capital investment into biopharma companies here, up 70% from 2020, which was already a record-breaking investment year," commented Kendalle O'Connell, president and COO of MassBio, a non-profit based in Cambridge that aims to help grow the industry. "There are 20 million square feet of lab and biomanufacturing developments in the pipeline between 2021 and 2024, and that expansion is expected to create 40,000 net-new jobs. We have the most robust early-stage biotech ecosystem of anywhere in the world. Our core focus is to support early-stage biotech companies that are working on the riskiest, breakthrough, cutting-edge science."

Looking ahead, O'Connell hopes to help broaden the industry engine beyond Boston and Cambridge, focusing on developing a talent pipeline that taps into a larger pool. As the state's life sciences sector grows, it will continue to be one of the most exciting geographies to watch as a barometer of global innovation.

### New Jersey

New Jersey has a long history in the life sciences – no less than 135 years. Its amplitude of skilled labor and research institutions combined with a continuous stream of start-ups, broad manufacturing capabilities, and global transportation networks allow the state to claim the title of the "medicine chest of the world."

Indeed, according to the HealthCare Institute of New Jersey, the state holds the highest concentration of scientists and engineers per square mile in the country, and is in the top two when it comes to the number of facilities that manufacture FDA-approved products. With both the talent and the resources to thrive, New Jersey is an epicenter of discovery.

14 of the world's largest 20 research-based biopharma companies maintain a significant presence in the state, as do 11 of the 20 largest medical technology companies. As such, New Jersey's economy is impacted enormously by the health of the sector. In 2021, biopharma and medtech companies generated US$120.9 billion in economic impact, accounting for 19% of the state's GDP. The industry has spawned 430,000 life sciences-supported jobs — more than one in 10 of all jobs in the state.

Debbie Hart, president and CEO of BioNJ, a non-profit that brings together industry members throughout the state, points to the fact that nearly 40% of all new FDA approvals throughout the pandemic have come from companies with a footprint in New Jersey as proof that her state continues to lead the way in introducing new therapies to the market.

Hart is particularly optimistic about New Jersey's life sciences industry given the state's current administrative posture with the reelection of Governor Phil Murphy for a second term in November 2021. "He is incredibly dedicated and inspired by making a difference in terms of innovation and we continue to see the positive impact of this," said Hart. "We are seeing more companies moving their operations to NJ, more companies being created in NJ, and increased funding due to the state government's commitment to innovation."

The financial, industrial and academic resources of New Jersey make the state a force to be reckoned with.

### Pennsylvania

New Jersey may have a large footprint in the life sciences, but so does its neighbor Pennsylvania. With its own ecosystem of biotech, medtech and pharma companies, research universities, and financial inflow, Pennsylvania is remarkable for a tradition of collaboration.

Many fundamentals of the life sciences were born in Philadelphia, the home to the first hospital and medical school in the nation. The state is at the pinnacle of academia for healthcare-related pursuits and hosts a plethora of colleges and universities (even more than Boston, and with a higher graduation retention rate as well), providing much in-demand talent for the sector. Industry-advancing innovations such as CAR T-cell therapy and mRNA vaccines started out as mere ideas in the City of Brotherly Love. 13% of the total workforce is employed in healthcare. According to San Francisco-based organization Health Evolution, Philadelphia's expansive hospital systems generated over 660,000 jobs statewide in 2019, contributing US$143 billion to the economy.

The Pennsylvania Biotechnology Center (PABC) helps to foster an environment of growth for innovators both resident to the state and drawn in from outside due to the region's robust ecosystem. Louis Kassa, current EVP and COO of the center (who will become CEO and president in July 2022) believes many start-ups find success thanks to the PABC's model whereby senior companies stay to help provide younger ones with the know-how and equipment to succeed. According to Kassa, while the timeframe of a successful exit for an early-stage life sciences company is 8.5 years on average nationally, the PABC has decreased this to 3.5 years.

"Of my eight years in Pennsylvania biotech, now is a particularly exciting time for the industry," said Kassa. "For the first time, we are seeing national players come to Doylestown due to the talent level and infrastructure we offer, including companies from Princeton, Boston and different places in California. The greater Pennsylvania region has always done well as a cluster, but if this current trajectory continues, we are at a tipping point of really making a big splash on the national scene."

Overall, East Coast states like Pennsylvania, New Jersey, and Massachusetts may be veterans of the nation's life sciences industry, but they are showing no signs of slowing down. ■

> With nearly 40% of all new FDA approvals over the last two years coming from companies with a footprint in NJ, our state continues to lead the way in bringing new therapies and cures to patients.

# Debbie Hart

President & CEO
**BIONJ**

**Can you give an overview of BioNJ's activities and performance over the past year?**
The theme has been flexibility. BioNJ spent significant time collaborating with government making sure that our members had what they needed in terms of Covid education. In terms of public policy, we worked to ensure that government is supporting industry and that innovation and access are protected. With regards to education and networking, we had to adapt and we adopted a completely virtual way of interacting. We have also continued to ensure that our members attain cost savings on a wide variety of essential services and have access to talent. We have also been laser focused on health equity, making sure that everyone has equal access to healthcare and medicines.

**Have you felt a palpable change following the administration change?**
New Jersey's (NJ) governor was re-elected for a second term in November 2021. He is incredibly dedicated and inspired towards making a difference in terms of innovation. We are seeing more companies moving their operations to NJ, more companies being created in NJ, and increased funding due to the state government's commitment to innovation. However, we are concerned with a number of proposals at the state level and what they may mean for innovation and access for patients and will be reviewing and monitoring them as we move forward. In addition, we are anticipating challenges on the policy front at the federal level as well. Changes proposed by the President and the new congress have the potential to harm innovation and patient access.

**What key policies and regulations are under review?**
It will be interesting to see in which direction the new FDA commissioner, Robert M. Califf, will move as he has previous experience and will be able to hit the ground running. It will also be interesting to see whether or not impactful things that came out of Covid, such as emergency use authorization (EUA), streamlined clinical trials and remote clinical trials, will be able to continue and improve the affordability of healthcare. There are proposals in different states across the country, including NJ, for a prescription drug affordability board (PDAB), and we are very concerned about the impact a PDAB could have on the number of companies being created, the funding making its way to companies, and ultimately the number of drugs making it to market and patients' ability to access that innovation.

NJ still stands out in terms of investment and the impact and nature of the various programs in the state. The NJ Innovation Evergreen Fund (NJIEF), being launched by the NJ Economics Development Authority later in 2022, has the intention to bring additional venture capital to the state through a public-private partnership where capital investment by the state is intended to be matched by private companies.

**How will the biopharma sector navigate skilled labor shortages?**
The talent shortage is a critical challenge that was exacerbated, but in some ways also addressed, by the pandemic. Companies can now recruit from around the world as people can be located anywhere and work remotely. We are, however, in a situation where many companies were formed during the pandemic and the talent pool just cannot keep up with the requirement. NJ has initiated the Pathways to Careers program, a collaboration between the NJ Department of Labor and Workforce Development and the NJ Community College Consortium, where academic partners, industry, and government are coming together to understand industry skill and talent requirements and work together to develop the required skills and talent for the future.

**Do you have a final message for our readership about BioNJ and NJ as a biopharma hub?**
In 2021, we were thrilled to see Governor Phil Murphy break ground on "The Hub" in New Brunswick, which will bring together industry, academia, government and investors in a physical space. Equally exciting is "The Cove", which is an even larger physical space with everything from housing, grocery shopping, industry, academia, government and investors – all in a walkable and waterfront complex.
With nearly 40% of all new FDA approvals over the last two years coming from companies with a footprint in NJ, our state continues to lead the way in bringing new therapies and cures to patients. ■





> We have the most robust early-stage biotech ecosystem of anywhere in the world.

# Kendalle O'Connell

President and COO
**MASSBIO**

**How has the Massachusetts life sciences evolved in the past few years and how is MassBio supporting them?**
2021 was a very exciting year for the Massachusetts life sciences ecosystem with US$13.6 billion of venture capital investment into biopharma companies here, up 70% from 2020, which was already a record-breaking investment year. There are 20 million square feet of lab and biomanufacturing developments in the pipeline between 2021 and 2024, and that expansion is expected to create 40,000 net-new jobs. We have the most robust early-stage biotech ecosystem of anywhere in the world.

Our core focus is to support early-stage biotech companies that are working on the riskiest, breakthrough, cutting-edge science. We are a leader around diversity, equity and inclusion, and we focus on creating pathways for our 1,500 member companies to prioritize DEI within their organizations. In August of 2020, we had a CEO pledge letter with over 200 commitments. Recently we conducted a survey of those companies to assess their DEI progress, resulting in the first ever set of Massachusetts data about diversity, equity, and inclusion in the Massachusetts life sciences industry.

**Could you tell us about MassBio Innovation?**
MassBio Innovation is one of our leading initiatives designed to support the entrepreneurial and early-stage life sciences ecosystem. Through our Partnering Days program we provide unique opportunities for established biopharma, medical device, or digital health companies to connect with leading early-stage companies and academic institutions developing breakthrough life sciences technologies. Also, 2021 was the first year that we launched 'Partnering Week', expanding upon Partnering Days by giving start-ups access to five established biopharma companies over the course of a week. Sponsoring companies of Partnering Days or Partnering Week have the opportunity to share what their partnering strategy looks like, showcase the science that they are working on, and establish new relationships with up-and-coming biotech companies.

**How are skilled labor challenges in the sector being addressed?**
Massachusetts has always been known as a place that puts out some of the best and brightest talent, but we really have to be thinking about what is next as the cluster continues to expand. We need to think outside of Boston and Cambridge and focus on building a talent pipeline for biomanufacturing and entry level positions. We need to regionalize our approach into all the emerging hubs of life sciences and tap into communities that have historically been underrepresented in the life sciences to create pathways into the industry. MassBio is working with the government and universities to understand the types of training that our industry companies will accept at all of the different levels. We also need to work on talent retention. To fill these 40,000 jobs we are going to have to take talent from all over the US and internationally.

**How has public perception of the sector shifted in the past few years?**
Public opinion is probably at an all-time high for the life sciences industry because of what happened through Covid-19. This was the first time in recent history that everyone in the world knew what it was like to live with an unmet medical need. And with the record-breaking development of multiple Covid-19 vaccines in less than a year, society better understands the amazing opportunities for patients that this industry can create. Looking forward, new technologies being researched now have the potential to offer patients not just treatments but cures. This is probably the most exciting time for patients in history.

**What is the outlook for MassBio and Massachusetts as a pharma and biopharma hub in 2022 and beyond?**
Massachusetts remains the best place in the world for the life sciences. We did not get there by chance, and we will not stay that way without proactive efforts. At MassBio, we are focused on a range of programs and initiatives to keep that leadership position, including efforts to expand biomanufacturing across the state, grow and diversify our talent pool, and continue to provide programs and services to support entrepreneurs and emerging biotech companies. The density of small and emerging biotech companies has attracted 18 of the top 20 biopharma companies in the world to establish a physical presence here. MassBio remains focused on providing the necessary support to help companies succeed so we can continue to stay the best place in the world for life sciences. ■

> Our blueprint to success has manifested in six IPOs and over US$3 billion worth of company value created.

# Louis Kassa

EVP & COO
**PENNSYLVANIA BIOTECHNOLOGY CENTER (PABC)**

**Can you give an overview of Pennsylvania Biotechnology Center (the PABC)'s mission and key activities over the past year?**

The PABC is a non-profit that offers state-of-the-art laboratory and office space to early-stage biotech companies. As the only incubator located in the heart of the pharma belt, home to 70% of all US pharma, we have been at full capacity for a decade. Our blueprint to success has manifested in six IPOs and over US$3 billion worth of company value created.

Our model continues to prove its value. The national average of a successful exit for an early-stage life sciences company is 8.5 years. At the PABC, this is decreased to an average of 3.5 years, as demonstrated by an independent study conducted in 2019.

**How does the PABC's model support young companies?**

We play close attention to the ecosystem – we do not take companies on a first come, first served basis as many incubators do. Rather, we seek diverse capabilities such that if you are a microbiologist in need of medical chemistry, for example, you can simply go across the hall for help given the flow cytometry, diagnostics, and medical devices on site. Around 70% of the companies in the PABC do small molecule drug translational research, but we also have a medical devices company, a dry eye disease company, and a diagnostics company.

Another differentiating factor of the PABC is we do not kick companies out, as we recognize the value senior companies play in providing young companies with experience and equipment. Many senior companies have serial entrepreneurs who have already commercialized; we have eight scientists onsite with FDA-approved drugs on the market, providing an unparalleled ecosystem in the incubator space.

**What facilities and services does the center provide?**

Today, we have a 150,000 square feet campus on 14 acres of land, with 30,000 square feet of lab space. We recently completed construction of a US$20.7 million facility with lab space, offices, and an event area. In January 2022, we opened a new facility in University City, Philadelphia, with our partners, Brandywine Realty Trust, that is currently at 95% capacity.

The PABC offers ample services and equipment with no upcharge, so when a young company looking to get started comes in, they do not need a big budget. Additionally, if a company gets stuck financially, we provide resources to get them unstuck by providing a funding opportunity through our tremendous network. We are about to close a US$50 million raise for our Hatch BioFund, an early-stage life sciences venture fund.

**How did the PABC companies respond to Covid-19?**

The PABC has both a flow cytometry and serologic company in our center. When the pandemic hit, having a serologic company drawing blood and doing clinical trials was tremendous, as seven of our companies pivoted to Covid-related initiatives. We were able to come up with some of the first Covid-19 tests in the country to be used in nursing homes and for first responders, ultimately providing antibody tests as well.

**What is your assessment of the health of Pennsylvania's biotech industry?**

For the first time, we are seeing national players come to Doylestown due to the talent level and infrastructure we offer, including companies from Princeton, Boston, and different places in California.

The greater Pennsylvania region has always done well as a cluster, but if this current trajectory continues, we are at a tipping point of really making a big splash on the national scene, particularly in the cell and gene therapy and regenerative medicine areas. It helps that within 50 miles there are 88 universities and colleges producing significant talent to help feed the system.

**What is your strategic vision for the PABC for the next 10 years?**

The PABC has the opportunity and vision to carve out a biotech quarter in Doylestown. When companies graduate from an incubator, there is the risk that they relocate, but surrounding the PABC's facilities is property prime for development. Companies can enjoy the support of the state and the PABC, and if we can get everyone working and growing together, we can increase job opportunities from 400 to 4,000.

I also see the opportunity to go into other clusters with our unique model, and we would love to see other incubators in major markets such as Boston and San Francisco using our platform, hopefully generating the same success. ■





# The West Coast

## The San Francisco Bay Area, San Diego, and Los Angeles

Each year, global commercial real estate company JLL publishes a ranking of the top life sciences clusters in North America considering factors including talent, innovation, and lab real estate. While Boston remained at the top of this list in 2021, the next two top hubs were thousands of miles away – San Francisco and San Diego.

The life sciences industry in California, having experienced an explosion of growth over the past several years, was well-positioned to play an instrumental role in the fight against Covid-19. Before the pandemic, for example, diagnostics was far from being a particularly lucrative field of biotechnology. Yet for years several companies throughout California worked behind the scenes to advance the diagnostics arena, particularly through advancing mRNA-related research. When Covid-19 first made headlines, these companies were able to shift their diagnostics technologies quickly towards the development and production of Covid-related tools.

The level of industry readiness that had been built up over decades in California and could be harnessed nearly immediately to combat the virus speaks volumes about the amount of research and innovation emanating from the state as well as the perennial importance of supporting this line of work.

### The San Francisco Bay Area

The birthplace of the biotech industry, San Francisco and its neighboring communities continue to outpace nearly all other regional clusters by a longshot. With the convergence of tech, biotech, and medtech, the region breeds innovation that is poised to shape the future of healthcare.

The Bay Area has a generous amount of infrastructure to accommodate the sector, yet it never seems to be enough. As of 2021, San Francisco had over 1.9 million square feet of leased lab space, with lab vacancies below 5%. The significant growth in startup activity that has generated this demand for space does not appear to be slowing down. According to David Schaffer, director of the Berkeley branch of QB3, a state-funded, multicampus entity that promotes innovation and entrepreneurship in the biosciences and spans facilities at UC San Francisco, UC Berkeley and UC Santa Cruz, there are various factors working in tandem to create an environment so conducive to growth. "To be a successful hub for bio innovation a region must have strong biological and physical sciences, engineering, medical schools and academic hospitals, and biotech and pharma companies," explained Schaffer. "There are two epicenters with that kind of confluence, Boston and San Francisco, and these regions lead the biotech industry on a national and perhaps global level."

Schaffer, also a professor at UC Berkeley, has noticed some encouraging changes in the interplay between universities and industry throughout his tenure. He sees this shift as making a positive impact on the number of novel therapeutics being produced in the region. "When I first started in academia, people who patented their discoveries were sometimes perceived as corporate sell-outs," said Schaffer.

He came to see the danger in hoarding discoveries within an ivory tower. With no collaboration with the private sector, his lifetime of work in a research lab could never have a direct impact on the wellbeing of a patient. As a result, he started to spin out companies based on technologies created by students and post-docs, eight of which are currently being used in human clinical trials.

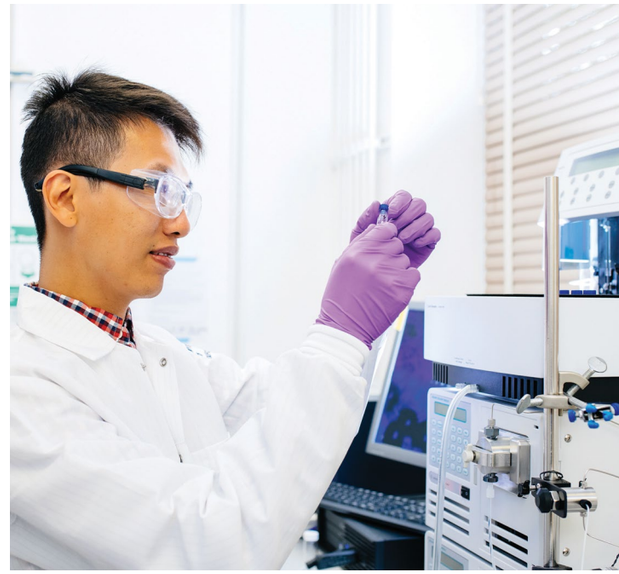


Image by Elena Zhukova, courtesy of QB3.

Image by Elena Zhukova, courtesy of QB3.

Schaffer points to Bakar Labs, a recent collaboration between QB3, UC Berkeley and the Bakar Bioenginuity Hub resulting in 40,000 square feet of lab space at the edge of the campus as a hallmark example of the mutual benefits gained from breaking down pre-existing barriers. "This proximity offers a win-win-win scenario," he explained. "The campus benefits as students and professors have the gratification of seeing their technologies take the next steps towards benefitting society; students and post-docs can learn how to conduct research in an industry setting, potentially leading to employment opportunities; and the companies enjoy access to scientific knowledge, new technology and people."

**San Diego**

Further south along the Californian coastline sits another hub that plays a major role in the overall health of the life sciences in the US: San Diego. The industry began here back in the late 1970s and has witnessed an explosion of new early-stage companies in recent years. The city has added more than 2.7 million square feet of infrastructure since 2016 to make room for this expansion. As of late 2021, San Diego had over 22 million square feet of lab exclusive space, with vacancy at 4.4%. Commercial real estate agency CBRE estimates that current demands are over three times higher than the amount of space that will be available over the next year. Funding the companies driving this demand, venture capital investments reached US$697 million within the fourth quarter of 2021, over US$520 million of which went to biotech and pharma.

Just as QB3's Berkeley branch facilitates growth in the Bay Area, UC San Diego's research capabilities have proven to be a main driver of innovation in the city. According to Joe Panetta, president and CEO of Biocom California: "UC San Diego is one of the most preeminent research universities, and its notoriety and success with technology transfer leads to new company creation."

**Los Angeles**

Los Angeles does not receive as much attention for its life sciences innovation as its counterparts to the north and south, but this may be about to change. The city has a strong track record of producing novel products that reshape the landscape, including synthetic insulin, open heart surgery, the paramedic system of responding to emergencies, and certain consumer health products including the nicotine patch. It has state-of-the-art hospital facilities, including Cedars-Sinai, home to its own business accelerator, as well as incubator spaces and accelerator programs like Cal State LA BioSpace and Heal. LA, powered by the Larta Institute.

Los Angeles historically receives less venture capital funding than other California clusters, especially compared to the Bay Area, but the balance has started to shift. The city currently receives ample funding from the National Institute for Health – US$1.15 billion as of 2021 – and the US$320 million fund inaugurating the creation of LA-based Westlake Village BioPartners in 2018 received another US$500 million near the end of 2020. These financial investments have translated into employment opportunities; the roughly 2,900 life sciences-focused establishments in the city support around 200,000 jobs locally.

This level of funding has allowed the sector to blossom. "A few years ago, there were only a handful of large life science companies in the region," commented Panetta of Biocom California. "Gilead Sciences' acquisition of Kite Pharma for US$11.9 billion produced a new crop of serial entrepreneurs and other talent, leading to the launch of new companies."

Overall, California gives the East Coast a strong run for its money in terms of innovation, funding and talent. While it is entertaining to compare the two coasts, however, the truth is that collaboration within and across hubs on both a national and global scale is what enables the industry to achieve such triumphs as its swift response to Covid-19. It will be this collaboration between regions and actors that will continue to drive forward a sector committed to helping people live longer, healthier lives. ■





> Whether it's therapeutics, food technologies, or solutions to environmental challenges, we believe that academic insights should not remain in an ivory tower.

# David Schaffer

Director
**QB3-BERKELEY**

**Can you introduce QB3 to our readers?**

QB3 began over 20 years ago as a state funded, multicampus entity to promote innovation and entrepreneurship in the biosciences, specifically biotech. The entity has four main components. The first three are the research branches at UC San Francisco, UC Berkeley, and UC Santa Cruz that create scientific knowledge, innovations, and networks. The fourth branch is the umbrella organization, known as QB3 Central, which takes basic discoveries from the campuses and fosters the translation of these technologies into companies that create products to benefit society as well as stimulate the state economy. The help QB3 provides includes access to incubator facilities, acceleration programs, funding, and networking with leaders in industry, venture capital, corporate law, and intellectual property law.

**How would you assess the current interplay between academia and industry?**

Historically, there has been a barrier in translating the incredible work done in academia into the private sector, which technologies need to reach to have a broad societal benefit. QB3 helps bridge this gap. For example, a collaboration between QB3, UC Berkeley, and the Bakar Bioenginuity Hub recently completed a new state-of-the-art biotech incubator called Bakar Labs with 40,000 square feet of lab space at the edge of the campus. Whether it's therapeutics, food technologies, or solutions to environmental challenges, we believe that academic insights should not remain in an ivory tower.

When I first started in academia, people who patented their discoveries were sometimes perceived as corporate sell-outs. I came to realize, however, that I could do laboratory research for the rest of my career in a way that would never make it to a patient. So I became involved in spinning out companies from our work, eight so far, and technologies created by students and post-docs in our lab are currently being used in eight human clinical trials. In general, academic sentiment has progressed in many ways to recognize the importance and mutual benefits of collaborating with industry.

**What types of companies enter Bakar Labs?**

There is a broad variety in the companies in our incubator. Pre-Covid, a large pharma company decided to terminate its antiviral program given the perceived weak market for antivirals. A member of the program licensed the technology from the company and set up operations in our incubator. In a different therapeutic area, a CRISPR-based company spun out of the Berkeley campus to develop treatments for human genetic diseases will soon be joining us. Additionally, one of my companies is currently in Bakar Labs developing advanced stem cell therapies. In particular, we have developed a scalable 3D system to mass produce stem cells and their differentiated progeny to serve as cell replacement therapies for a range of human degenerative diseases. Within the incubator, there is even a company focused on developing synthetic meats, which will improve the environmental effects of the food industry. This is just a small taste of the broad variety of companies that will be entering Bakar Labs.

**What is your opinion on San Francisco's emergence as a top hub for biotech innovation?**

To be a successful hub for bio innovation, a region must have strong biological and physical sciences, engineering, medical schools and academic hospitals, and biotech and pharma companies. There are two epicenters with that kind of confluence, Boston and San Francisco, and these regions lead the biotech industry on a national and perhaps global level. San Francisco was the birthplace of the biotech industry, and there continues to be explosive innovation here. There has been a significant growth in startup activity in the Bay Area, particularly over the past five years, and this activity makes the region an exciting place to work.

**How will QB3 shape its main initiatives moving forward?**

There are certain areas where the free market stimulates innovation in the private sector, such as human health and digital technologies. However, there are also areas where the alignment between major societal need and free market incentives is not as close. Before Covid-19, vaccines were a great example of a relatively small margin, risky field, and it took a pandemic to change this outlook. Today, the free market does not incentivize innovation in several areas where this is great societal need. For example, antibiotic resistance is a challenge. Another example is biofuels – every time the price per barrel of oil shoots up, biofuels start looking competitive. When the price goes back down, however, interest is lost. QB3 greatly looks forward to continuing to support innovation in such societally important areas. ■

> We experienced explosive growth across the state and consequently adopted a new name: Biocom California.

# Joe Panetta

President & CEO
**BIOCOM CALIFORNIA**

**What have been the key advancements in Biocom California's operations over the past few years?**

We experienced explosive growth across the state and consequently adopted a new name: Biocom California. Our new brand reflects our leadership as the statewide trade association for the life sciences with more than 1,600 members in key life science clusters across California. We provide our members with advocacy, connections to capital, workforce development, an expanding talent pipeline, and networking opportunities in a state that has the largest concentration of life science companies in the world. Further east, Biocom California expanded its presence in Washington D.C., strengthening our policy expertise in FDA and CMS to complement our historical relationships with Congress and the executive branch.

On a regional level, we have seen an explosive growth in each of our clusters. In the San Francisco Bay Area, we see major companies like AbbVie, Thermo Fisher Scientific and Merck create large facilities in South San Francisco, the birthplace of biotech. In the greater Los Angeles region, we see organic growth and the rise of venture capital players. A few years ago, there were only a handful of large life science companies in the region. Gilead Sciences' acquisition of Kite Pharma for US$11.9 billion produced a new crop of serial entrepreneurs and other talent, leading to the launch of new companies. In San Diego, we have a growing abundance of new early-stage companies. UC San Diego is one of the most preeminent research universities, and its notoriety and success with technology transfer leads to new company creation.

Biocom California is also addressing a critical challenge. We must attract more talent to our industry – more researchers, business professionals, entrepreneurs, and future executives. And it needs to be diverse talent. In 2021, Biocom California launched a major Diversity, Equity and Inclusion initiative, leading to the rollout of our statewide DE&I member CEO pledge.

One of the key drivers of the future of healthcare will be the convergence of tech, biotech, and medtech. We believe that Silicon Valley and the life science ecosystem are uniquely positioned to address the future of healthcare. Our new Tech+Biotech+Medtech community aims to capitalize on existing expertise by creating opportunities for experts from the three sectors to come together to realize the full promise of digital health.

**How would you assess the industry's response to Covid-19?**

The speed at which the industry capitalized on several years of mRNA research to develop vaccines and partner with the FDA to get these through the regulatory review process was incredible. Many companies in California had already been working in the diagnostics arena, which was not the most lucrative field of biotechnology pre-Covid. These companies quickly shifted their diagnostics technologies towards pandemic-related needs.

Through the pandemic, we helped our members access the supplies and regulatory knowledge necessary to continue working. Biocom California assembled a statewide Covid-19 task force, bringing together experts from various fields including HR, facilities management, environmental health and safety, legal, and government affairs, to provide a one-stop comprehensive guidebook for our members.

**What advancements has California made in the precision medicine space?**

California has made great progress in precision medicine and our members lead the way in genetic sequencing, data analytics, and cell and gene therapy. Regenerative medicine is also growing – a few years ago, we were able to renew the California Institute for Regenerative Medicine's funding at US$5.5 billion so it could continue to provide grant funding to California-based companies developing technologies using stem cell research to treat patients in a more targeted way.

**As we head into a post-pandemic world, where will Biocom California focus its efforts?**

We want patients to have access to affordable medicines, which entails partnerships between industry, government, and other entities like PBMs, insurance companies, and hospitals.

Biocom California worked with laser-focus to defeat HR3, a bill in the House of Representatives that proposed to import foreign price controls on biopharmaceutical products, potentially destroying market competition that has rewarded biotech investment in the US and resulted in the introduction here of the most revolutionary therapies in the world.

Additionally, Biocom California values its partnerships with global entities, such as our 10-year relationship with Japan. We continue to look at regions with strong life science industries that could be potential partners and prioritize positioning the California life science industry on the world stage. ■

# DRUG DISCOVERY AND DEVELOPMENT

"We know vaccines can lead to higher quality, longer lives, but wide acceptance and uptake, in addition to an adequate supply chain and access, need to occur for vaccines to be effective for the global community."

**- Candice Long,**
**President – US Infectious Diseases & Vaccines,**
**Janssen Pharmaceuticals**



Image courtesy of CordenPharma

# Therapeutic Fields on Fire

## Advancing CNS treatment

The central nervous system (CNS), which has enjoyed attention within the life sciences research landscape for years, became even more prominent with Covid-19.

In 2020 and 2021, significant investor funding flooded into CNS research for both new companies and big pharma alike. Innovation within the space also took on a renewed importance: the pandemic and the stress it brought along led to a spike in the number of people suffering from depression, anxiety disorders, PTSD, and other mental health conditions.

According to Emer Leahy, president and CEO of PsychoGenics, there has been an acute rise in the ubiquity of mental health disorders. "This has been particularly evident in the vulnerable adolescent population which showed an approximate 30% increase in the prevalence of mental illness compared to prior years," said Leahy. "Social isolation, fear and limited access to treatment as a result of the pandemic have triggered a mental health crisis."

In addition to its preclinical CNS-focused CRO work, PsychoGenics has been working on a platform that uses AI in phenotypic drug discovery. With SmartCube, the company has built up a library of over 7,000 chemically diverse compounds that are potential starting points for new drug discovery programs.

Contributing to the neurodegenerative disease space, AC Immune is a clinical-stage biopharmaceutical company leveraging its proprietary SupraAntigen and Morphomer technologies to generate highly specific biologics and small molecule drugs for Alzheimer's disease, Parkinson's disease, and certain rare indications. "The neurodegenerative field is moving towards precision science and diagnostics," commented Andrea Pfeifer, the company's CEO. "Identifying and targeting these misfolded proteins and related pathways in patients will be key to achieving the best possible treatment."

Ultimately, as is the case across the board for companies developing novel therapeutics, their molecules must pass the test of receiving regulatory approval. According to Robert Fremeau, chief scientific officer of Vyant Bio, CNS-related treatments face a particular challenge: "Most drugs fail in the clinic not because of toxicity or safety concerns, but due to a lack of efficacy. This is especially true for CNS drugs where the available animal models have such poor predictive validity."

For this reason, Vyant Bio has a drug discovery platform that combines human patient-derived organoid models of brain disease with machine learning. The company believes its human-first approach is better suited for the discovery of complex neurological and neurodegenerative disorders. As Jay Roberts, president and CEO of the company noted, "there is an emerging trend of using very innovative technologies including data science, AI, and machine learning, combined with strong biological systems. Combining science and strong biology allows for good decision making around identifying therapeutics that ultimately will become safe and effective treatments for patients."

As CNS-related disorders continue to pose significant unmet medical needs, companies leveraging innovative technologies are pushing the needle forward.

### Covid-19 provokes innovation in cell and gene therapy

Cell and gene therapies and gene editing tools such as CRISPR have progressed significantly over the past several years, but the pandemic created a sense of urgency that boosted funding from governments and private investors, as well as introduced the field into public discourse. As Covid-19 vaccines first rolled out, innovative techniques such as mRNA technologies became a part of household conversation for the first time. Most experts agree the pandemic created such a need for both the regulatory approval and implementation for this type of vaccine that the field leapfrogged a decade's worth of progress.

> Combining science and strong biology allows for good decision making around identifying therapeutics that ultimately will become safe and effective treatments for patients.
>
> **– Jay Roberts, President & CEO, Vyant Bio**

When news about Covid-19 vaccines first reached the public, many onlookers did not understand the science and formed hasty conclusions about their safety. The main point of confusion regarded the fact that mRNA vaccines are incapable of altering the patient's genetic material as the mRNA content never enters the nucleus of the cell where DNA is located. Some people were also confused about the use of viruses in the form of viral vectors, which are a popular part of a molecular biologist's toolbox when looking to deliver genetic material into cells.

Janssen Pharmaceuticals' Covid-19 vaccine program leveraged the company's AdVac technology, which is based on the development and production of adenovirus vectors. "Adenovirus vectors are genetically altered forms of an adenovirus that lack the DNA needed to replicate, so the vaccine cannot cause a cold," explained Candice Long, president of US infectious diseases and vaccines at the company. "In the case of the Covid-19 vaccine, the immune system of someone who receives our vaccine recognizes the Covid spike protein as foreign once it enters their cells, producing antibodies and activating T cells to target it. This allows the individual's immune system to recognize the SARS-CoV-2 spike protein and be ready to defend against it."

While some people remained skeptical, many recognized the pandemic and rapid deployment of such vaccines to be valuable insight into the future of inoculations. As Faith Salamon, a Pfizer spokesperson noted, their company will build off its current mRNA technology in the exploration of other programs: "The approval of the first mRNA-based Covid-19 vaccines was a scientific turning point, establishing mRNA as a versatile, flexible technology. The focus and drive Pfizer gave to developing our Covid-19 vaccine in partnership with BioNTech gave us a wealth of scientific knowledge in just one year. Pfizer's next wave of mRNA scientific innovation is expanding in the infectious disease arena with development programs in flu (influenza) and shingles, also exploring its versatility in the areas of rare genetic diseases."

Taking the approach to the next level, Arcturus Therapeutics, a late-stage clinical messenger RNA vaccine and therapeutics company, saw benefits in bringing self-amplifying mRNA into the development of a Covid-19 vaccine. mRNA vaccines that enter the recipient's body via intramuscular injection express an antigen that provokes an immune response. Conventional mRNA vaccines elicit an antigen expression period of only few days before the mRNA molecule degrades. Self-amplifying mRNA, on the other hand, produces a longer expression period, allowing for dose levels to be dramatically lower. Arcturus Therapeutics' lead Covid-19 vaccine candidate has only 5 micrograms per dose, for example. The lowering of dose levels helps reduce safety risks associated with higher doses. It also makes vaccines faster and more efficient to manufacture at scale.

Joseph Payne, the company's president and CEO, sees promise in the speed at which the space is evolving. "Over the last two years, we moved swiftly from conventional mRNA to self-amplifying mRNA, as opposed to each one taking 10 years to develop and implement," he explained. "We hope the self-amplifying mRNA will be a more durable vaccine with broader variant coverage, which is desirable as we transition into an endemic booster market."

Covid-related advancements are also being made within the gene editing space. Mammoth Biosciences has pioneered work with CRISPR-based diagnostics and is working to augment the toolbox of CRISPR proteins to provide novel delivery possibilities. According to the company's CEO Trevor Martin, CRISPR can be used as a search engine for biology in the sense that CRISPR proteins can be

**Insmed developed a drug-device combination that became the first approved therapy to treat patients with a refractory form of a rare and serious lung infection.**

# Will Lewis

Chairman & CEO
**INSMED**

**Could you update our readers on how 2021 was for Insmed?**
In 2021, the company expanded upon the growth it experienced in 2020, which had been the most significant year in the company's history to date. As a company focused on rare diseases, Insmed is currently pursuing four different pillars. Our first pillar and lead program is now approved in the US, Europe and Japan, and has commercially launched. We have advanced our other two development programs, both pulmonary-related, and we added our fourth pillar focused on translational medicine.

**Can you provide more insight into the process of bringing your commercial drug to the market?**
Insmed developed a drug-device combination that became the first approved therapy to treat patients with a refractory form of a rare and serious lung infection. We are now evaluating this therapy in a frontline patient population, with two clinical trials that are underway.

**What is the status of Insmed's second and third pillars?**
The company's second pillar, brensocatib, is currently in a phase 3 clinical trial as the first investigational DPP1 inhibitor developed for neutrophil-driven inflammatory conditions. We aim to enroll more than 1,600 patients globally in the study to address bronchiectasis, a pulmonary condition that currently has no approved treatments. The drug is unique in that it targets the inflammatory process associated with bronchiectasis rather than the historically unsuccessful approach of treating with anti-infectives. Results from the phase 2 trial were published in the New England Journal of Medicine, the first time in nearly 20 years this journal has published on bronchiectasis. Given the mechanism the drug utilizes, we are evaluating or plan to study it in several other diseases such as cystic fibrosis, chronic rhinosinusitis without nasal polyps, and hidradenitis suppurativa.

Our third pillar is treprostinil palmitil inhalation powder (TPIP), a novel, investigational formulation of prostanoid, a class of drugs used for the treatment of pulmonary arterial hypertension (PAH). PAH is a serious, progressive, rare disease involving narrowing and constriction of the pulmonary arteries, making it difficult for the heart to pump blood effectively. TPIP relaxes the vasculature in a pulmonary setting. We currently have three phase 2 programs underway to evaluate the efficacy of TPIP in PAH and pulmonary hypertension associated with interstitial lung diseases.

**What work is Insmed doing in the translational medicine space?**
Our fourth pillar is translational medicine. In 2021, Insmed acquired three small companies with teams that are leaders in the fields of gene therapy, protein engineering, and protein manufacturing. This has augmented our existing research capabilities to develop the next generation of medicines utilizing cutting-edge technologies. Insmed wanted to develop an engine that could continuously produce impactful medicines to address rare and serious diseases and write the future of the company. Currently, we have close to 10 pre-clinical programs running and expect to have at least one IND filed every year for the next several years.

**Has Insmed faced any supply-chain challenges related to Covid-19?**
Before the pandemic hit, we had already decided to invest in strengthening our supply chains because we see it as a corporate responsibility to have redundancy within your supply chain if you are in the world of pharmaceuticals. Not all materials are available in the US, so it is important to create inventory supply. We could not have anticipated a global disruption as severe as the pandemic, but our strategy has allowed us to avoid any significant disruptions for Insmed along the way.

The concept of globalization as an unfettered path which everyone is going to pursue has certainly been challenged over the past two years, first with the pandemic and now with increasing geopolitical turmoil. This changes the way companies regard just-in-time production and the origin of raw materials.

**Can you elaborate on Insmed's Investigator-Initiated Research initiative and what it means for the life sciences space?**
At Insmed, we follow the science. The idea behind our investigator-initiated research program is to be responsive to key opinion leaders around the world who have ideas for how our therapies may be able to help patients. We want to support innovation in the life sciences ecosystem and will provide financial support and/or product supply for novel research proposals that answer important scientific and medical questions in our areas of interest. In some cases, we will even take on an investigator's proposed research idea as inspiration for a study of our own. ■





Humans have approximately 2,000 microRNA's regulating the expression of 20,000 genes. In theory, one microRNA can regulate 100 mRNA's at the same time by recognizing a binding site in the mRNAs it is regulating and thereby influencing their respective translation to proteins.

**– Roel Schaapveld, CEO, InteRNA Technologies**

programmed with a guide RNA that targets a specific genetic sequence before using its built-in scissors to edit the genes in question.

Mammoth Biosciences had been interested in the realm of CRISPR-based diagnostics since its founding and was able to leverage its previous work to help combat the spread of the virus. "While it was impossible to have foreseen Covid-19 as a specific target, we always believed in the accessibility of testing for infectious diseases," explained Martin. "Hence, leveraging the technology to address the pandemic was a natural progression, evidenced by how quickly we published the first available data of a CRISPR-based test for Covid-19."

Martin is optimistic about the potential impact of this type of testing not only for Covid-19 but also for future pandemics, given the broad accessibility the platform offers. Additionally, CRISPR-based diagnostics can be created quickly in response to new variants.

The technology driving CRISPR has the ability to increase accessibility across the spectrum of testing, whether it be in the lab or the doctor's office or ultimately within the patient's home. In this manner, the diagnostics tool presents a win-win for users—Martin sees the potential for this type of tool to be accurate like a PCR test while also accessible like an antigen or antibody test.

The power of cell and gene therapies also lies in malleability. Speaking of the power of miRNA in particular, Roel Schaapveld, CEO of InteRNA Technologies, a clinical-stage biotech company developing a pipeline of RNA therapeutics to target human diseases like cancer, acknowledged: "Humans have approximately 2,000 microRNA's regulating the expression of 20,000 genes. In theory, one microRNA can regulate 100 mRNA's at the same time by recognizing a binding site in the mRNAs it is regulating and thereby influencing their respective translation to proteins."

To accommodate the rise in cell and gene therapies, there are CDMOs that specialize in this line of work. Forge Biologics, for example, is currently working to expand its adeno-associated virus (AAV) manufacturing capabilities to better enable its clients to speed to the clinic. Timothy J. Miller, the company's CEO and president, anticipates increased growth. "I believe that in 2022 we will see more good stories come out in gene therapy, such as therapies getting approved, more approvals for reimbursement, and more positive clinical data coming out," he said. "AAV trials represent over 70% of the ongoing gene therapy trials, and thus, as a modality, AAV manufacturing is at a premium."

Covid-19 advanced cell and gene therapy by at least a decade, leading to an array of companies working in a wide range of therapeutic areas. With this push, the field will remain a hotbed for innovation once the pandemic has subsided.

**The power of proteins**
One way to unlock the power of proteins is to work with them directly. Chris Larson recognized that while proteins execute vast amounts of cellular functions, the cell's genome only codes for a few protein primary sequences. He helped found SNO bio to unlock the potential for drugs to manipulate the addition or removal of protein S-nitrosylation (SNO), as malfunctions in the protein can result in disease.

Larson sees immense potential in the enzymes from his company's target discovery platform. "Nature needs mechanisms to generate sufficient size and diversity in its protein tool kit to accomplish the huge variety of functions they need to execute," he explained. "Protein post translational modification provides this, driving the total number of different proteins in a cell over 1,000,000."

Proteins can also play a major role in fighting viruses, as discovered by Evrys Bio. Founded on discoveries from Princeton University that took a novel approach to antiviral therapy, the company's scientific focuses is on sirtuins, signaling proteins involved in metabolic regulation that help with intrinsic immunity on a cellular level. "Throughout evolution, cells have had to defend themselves against foreign DNA from viruses, and sirtuins are part of the cell's natural defense," explained president and CEO Lillian Chiang.

According to Chiang, two critical properties arise as a result of engaging the natural defenses of the cell: first, the unique approach seems to be effective against a variety of virus types, meaning treatment does not have to be designed down to the strain and can provide broad-spectrum coverage. Second, a sirtuin-based approach helps avoid the problem of virus mutations. This means that Evrys Bio's antiviral treatments have the potential to be broadly prescribed without the same worry for drug resistance.

As the industry invests in understanding the nuances of proteins and protein manipulation within the human body, our ability to use this approach towards treatment opens new doors to advancing the standard of care across a variety of therapeutic areas. ■

## Trevor Martin

Co-Founder & CEO
**MAMMOTH BIOSCIENCES**

**What prompted Mammoth Biosciences' entry into the diagnostic and therapeutic space?**
We are excited about augmenting the toolbox of CRISPR proteins beyond the initial systems like Cas9 for several reasons. First, we see potential for new products that can be built with the properties of these proteins, as evidenced in our pioneering work with CRISPR-based diagnostics. Second, we believe we can unlock new iterations of pre-existing therapeutic ideas through our pioneering of ultra-small CRISPR systems. These are systems that are physically smaller than the Cas9 and have important delivery implications to enable potentially new in vivo therapies.

**What are the benefits of Cas14 and CasΦ nucleases over Cas9 when it comes to genome editing?**
These systems are smaller, which allows for novel methods of delivery. We can start to achieve some of the holy grails of editing, like looking for permanent cures rather than just treatments. They also have a better targeting range. This is because CRISPR proteins have PAM sequences that limit where the individual protein can go. By having a more diverse PAM sequence the protein can go to more regions in the genome, which is particularly transformative when you want to make multiple edits on the same protein.

**What are the mechanics of your CRISPR-based high throughput Covid test?**
Fundamentally, the test leverages the idea of CRISPR as a search engine for biology. One can program CRISPR proteins with a guide RNA, which is a molecule that directs the search for a specific sequence, such as a gene that you want to edit to cure or treat a disease. This diagnostic technology works like a molecular shredder on a sample by cleaving tons of single-stranded nucleic acid when the Cas enzyme binds to the sequence its been programmed to identify, which, as a result, strengthens the test's signal. This ability to detect nucleic acids renders it a molecular test with a degree of sensitivity and specificity that rivals more standard tests like the PCR. ■

## Joseph Payne

President & CEO
**ARCTURUS THERAPEUTICS**

**Can you introduce us to Arcturus Therapeutics?**
We are a late-stage clinical messenger RNA vaccine and therapeutics company. For vaccines, our self-amplifying RNA, or STARR, addresses dose level issues by considerably reducing dose levels. For therapeutics, we address the challenge of safe and effective delivery of mRNA with LUNAR, our lipid nanoparticle delivery technology that protects and safely transports mRNA molecules to target tissues.

**Can you elaborate on how the STARR delivery technology?**
Conventional mRNA vaccines that enter the body through intramuscular injection express an antigen that elicits an immune response. The antigen expression usually lasts for about 2-3 days before the mRNA molecule degrades. Self-amplifying mRNA, however, has a longer period of expression. This longer expression period allows for significantly reduced dose levels, such as the 5 micrograms per dose that we have achieved for our lead Covid vaccine candidate.

We have the ability to lyophilize our vaccine products and remove the water component unlike other mRNA vaccines, which are shipped as frozen liquids, providing a more stable supply chain.

**How can the LUNAR delivery system be used for protein replacement therapies?**
For therapeutics we have to design for systematic administration of larger doses. It is important the mRNA is pure, and the delivery technology is biodegradable. If the delivery vehicles (lipid nanoparticles or LNPs) accumulate, it can pose risks to the liver or lungs, but LUNAR lipids have been shown to degrade after about 48 hours in pre-clinical studies.

We are currently working on a potential treatment for ornithine transcarbamylase (OTC) deficiency, related to the OTC enzyme in the urea cycle that helps process proteins and ensure normal ammonia levels. We can potentially replace the OTC enzyme by delivering its mRNA to liver cells. Once delivered, nature takes over and makes functional OTC enzyme that can potentially cure the disease and may prevent the need for liver transplants. We are also working on an mRNA therapeutic that can be inhaled to access the bronchial epithelial cells to treat cystic fibrosis. ■





## Shuang Liu

CEO & Founder
**CONSYNANCE THERAPEUTICS**

**What are the key molecules that make up ConSynance Therapeutics' pipeline?**
ConSynance is a clinical-stage virtual biopharmaceutical company focusing on rare diseases in the central nervous system, particularly those related to hypothalamic dysfunction. Our lead asset is CSTI-500, a small molecule first-in-class triple monoamine reuptake inhibitor (TRI) that I originally co-invented to treat depression before discovering its potentially benefit on patients with Prader-Willi syndrome (PWS) and hypothalamic obesity (HO). We recently received FDA approval to study CSTI-500 in PWS patients, which will mark the first clinical study involving this population. We plan to initiate the clinical trial in Q2 of 2022.

In 2021, we reached an asset purchase agreement with Harmony Biosciences for our second drug, (formerly CSTI-100, now renamed HBS-102.) This potential first-in-class molecule with a novel mechanism of action has the potential to treat a variety of neurological disorders. ConSynance currently holds the license of this drug for the Greater China region and Harmony has global commercialization rights outside of Greater China. Harmony is currently evaluating the potential of HBS-102 in a variety of rare neurological areas. ■

## Andrea Pfeifer

Co-Founder & CEO
**AC IMMUNE**

**With a vast pipeline of 11 therapeutics and 3 diagnostic product candidates, where does AC Immune place priority?**
Our pipeline is quite mature around three targets, Abeta, Tau, and a-syn, and our emphasis for 2022 is on delivering on clinical milestones. Out of the 11 therapeutics, we have eight clinical therapeutic products and expect to have seven clinical readouts within 2022. Given their promise, we are currently working to advance our phospho-Tau vaccine ACI-35.030, semorinemab anti-tau antibody, Tau-PET candidate, ACI-24 vaccine, crenezumab Abeta antibody, and our non-invasive diagnostic for alpha-synucleinopathies (e.g. multiple system atrophy). Regarding the latter, we have recently presented at the ADPD congress the first live human brain able to detect pathological alpha-synucleins.

**What does AC Immune hope to accomplish by the end of 2022?**
We will continue to develop strategies to preserve the quality of life of patients with neurodegenerative diseases with the main aim to prevent or delay the onset of AD in a safe and cost-effective manner. If our anti-Abeta monotherapy can do this, it will be a major breakthrough for AC Immune and the entire field.

We also hope to soon have a breakthrough in Tau inhibition with our antibody candidate semorinemab. Additionally, we are excited to show the first non-invasive diagnostic for alpha-synucleinopathies, which is a transformative step towards achieving our vision for developing precision medicines to treat neurodegenerative diseases. ■

## Lillian Chiang

President & CEO
**EVRYS BIO**

**Could you introduce Evrys Bio's alternative approach to antiviral therapy?**
Evrys Bio was founded on breakthrough discoveries from Princeton University that took a unique approach to antiviral therapy. The company's scientific core centers on the role of sirtuins, proteins that play a vital role in intrinsic immunity on a cellular level.

**Can you elaborate on the importance of sirtuins in treating viral infections?**
By engaging the natural defenses of the cell, two critical properties arise. First, this approach appears to be broadly effective against a variety of virus types. Secondly, it targets something fundamental to the cell biology that controls the virus, meaning there is no pressure for the cell to mutate around the effect of the drug.

When you start an antiviral company, the first question people have is which virus you will target, as this determines the market for your product. We approached this differently, hoping to create products that could address multiple viruses simultaneously while also bypassing the problem of drug resistance. If you can freely prescribe without worrying whether you are targeting the exact virus or whether there is a potential for drug resistance, the market expands drastically. Evrys believes it is at the forefront of a paradigm shift in treating infections. ■

**In 2021, we focused on introducing our green pathogen reduction technology to biotechnology and pharmaceutical companies.**

# Trevor P. Castor

President and CEO
**APHIOS CORPORATION**

**Could you provide some highlights of Aphios' operations throughout 2021?**
In 2021, we focused on introducing our green pathogen reduction technology to biotechnology and pharmaceutical companies. We developed a technique called critical fluid inactivation (CFI) to ensure that biologics and blood products critical for patient care are free of harmful viruses and other pathogens. CFI disrupts these particles by giving them the "bends", meaning it inactivates them without destroying the underlying biologic material.

We also focused on developing cannabis-based, pharmaceutical grade therapeutics utilizing proprietary manufacturing and nanotechnology platforms for disease states such as chemotherapy-induced peripheral neuropathic pain (CIPNP), substance use disorders, anxiety, and multiple sclerosis. Our goal is to mitigate physical and mental intrusions like pain, anxiety and depression that destabilize our internal endocannabinoid system. This is done by introducing external cannabinoids from cannabis or hemp to rebalance the system pharmaceutically. Moreover, we are nanoencapsulating specific pharmaceutical grade cannabinoids so they can be sustained in the body longer and released over time to change acute treatment by cannabis and cannabinoids to address chronic conditions such as CIPNP and anxiety.

**How would you assess the regulatory posture towards cannabis products under the Biden administration?**
It is too early to tell given the challenge of passing comprehensive legislation around cannabis. Congress will likely legalize the use of marijuana, but this will probably trigger significant senatorial pushback, to say nothing of securing presidential assent. Nevertheless, the overall tenor has been more mature than last year.

**What are the highlights of Aphios' current product pipeline?**
Our current pipeline includes our lead product, Zindol, used for chemotherapy-induced nausea and vomiting (CINV). We are expanding that pipeline to include products for first trimester pregnancy and anemia. The second major product is APH-0812 for HIV latency towards an HIV cure. The third major clinical program centers around Alzheimer's disease where we are developing a compound that we believe works because it satisfies both the necessary and sufficient conditions to manage amyloid plaques and stimulate synaptic regrowth. We also have several preclinical programs in prostate, breast and pancreatic cancer. Furthermore, we have good preclinical data and intellectual property coverage for kidney and liver transplantation as well as for diabetes through oral insulin.

**Can you elaborate on your different types of nanotechnologies for enhanced delivery?**
One aspect of the nanotechnology platforms is for the encapsulation of therapeutics including small and large molecules (small interfering RNA and mRNA) into lipid nanoparticles utilizing our green technology platform. This will typically be used for either intravenous or topical applications. Moreover, we can encapsulate both materials in the lipid bilayer and the aqueous core, as we have demonstrated in our HIV cure therapeutic.

The second of our nanotechnology capabilities entails the encapsulation of molecules into biodegradable polymer nanospheres, which degrade over time to release bioactive molecules in a sustained manner. This technology can be utilized mainly for oral delivery of proteins, intranasal delivery of compounds, and the intramuscular or subcutaneous delivery of vaccines. We are currently developing a combination technology to encapsulate lipid nanoparticles into polymer nanospheres for a single shot mRNA vaccine with improved shelf-life that will be capable of being stored at refrigerator or room temperature.

The third type of nanoparticle technology Aphios offers creates nanoparticles by, for example, taking an insulin crystal and breaking it up into smaller components. By creating a larger surface-to-volume area, we have enhanced insulin's efficacy as more active sites are exposed. This technology is applicable to both organic and inorganic molecules as we have shown for insulin and paclitaxel, improving the delivery of nanoparticles for sustained release.

**How have you found market reception for products that are more environmentally sustainable?**
The individual consumer loves these products, which is in stark contrast to big pharma companies who are against the implications these products have on their business model. Big pharma companies prefer to use synthetic roots because they can scale rapidly. We prefer to work with plants and microorganisms because they provide ecological balance and sustainability.

**Do you anticipate Aphios' approach towards more naturally derived products to become a trend within society at large?**
I believe it will. Food is a natural source of enzymes and nutrients, and dietary supplements and nutraceuticals are upgraded foods. It comes down to different volumes and concentrations of these products and how they impact our bodies. Thus, as more people become invested in managing their physical and mental health, there will be a higher utilization of natural products. ■





# Innovations Enhancing The Patient Experience

## Paving the way for new therapeutics to meet unmet medical needs

Image courtesy of Arcturus Therapeutics.

Innovative scientists are paving the way for new therapeutics to meet unmet medical needs. Equally important are advances being made that enhance the patient experience, particularly when it comes to the delivery methods of those molecules as well as more effective diagnostics testing.

### A new diagnostics frontier

Historically, blood samples were outsourced because complete blood counts (CPCs), tests that measure the quantity of different types of cells that comprise blood as well as provide information about their physical properties, were done in central labs. When CPCs were first performed, somebody had to manually count cells under a microscope. Then in the late 1960s, a German scientist developed a novel method to count and characterize cells that used lasers, not human eyes. When this method known as flow cytometry eventually took hold, it revolutionized the speed and efficiency with which blood tests could be performed.

In 2022, the diagnostics space is undergoing another revolution. Sight Diagnostics has developed its Sight OLO, a high-performance CPC analyzer that the company claims can provide lab grade results in minutes utilizing just two drops of blood. According to Yossi Pollak, the company's CEO: "This technology is essentially replacing the human eye behind the microscope."

The technology driving Sight OLO leverages machine vision and AI to collect and analyze over 1,000 images per blood sample. As the company continued to amass data, it realized it could do something with all the information it was gathering. According to Pollak: "We soon recognized that the ability to digitize blood samples and collect large amounts of blood morphology data could have a far greater impact than just CBCs, so we started to collaborate with pharma companies to develop companion diagnostics capabilities, providing them with tailored tools to streamline the clinical trial process for the development of new drugs."

Sight Diagnostics has partnered with hospitals and major pharma companies like Pfizer and is currently expanding into the companion diagnostics space. To its end, Karius, a California-based company also working to reshape the diagnostics landscape, has seen its Karius Test implemented in hundreds of hospitals. The test can help rapidly diagnose infections in patients and is particularly beneficial to

people undergoing cancer treatment, as they are likely to experience some degree of immunosuppression.

Like Sight Diagnostics, Karius uses technology to mitigate the invasive nature of diagnostics testing. "The unique advantage of our liquid biopsy test is that it does not require an invasive sample collection of infected tissue or fluid," explained Alec Ford, the company's CEO. "Instead, it detects small fragments of DNA from the pathogen causing the infection within the bloodstream. In this way we can find over 1,000 different pathogens from the site of the infection, irrespective of where the infection is in the body."

According to internal analysis conducted by Karius, approximately 60% of invasive diagnostics procedures could have been avoided if the Karius Test were used.

In addition to non-invasive alternatives to testing, patients are increasingly demanding privacy and convenience for tests, especially when it comes to the detection of sexually transmitted infections. binx health has developed a molecular platform that provides lab-quality test results in 30 minutes for chlamydia and gonorrhea, allowing for patients to receive diagnosis and treatment within a single visit. According to CEO Jeff Luber, this "test and treat" capability presents a solution to a demand exacerbated by the pandemic: people now more than ever want convenient solutions to care. With binx's tests patients have the option to collect samples from within the privacy of their own home. "When we think about how people consume healthcare, there are essentially two kinds of populations – those who show up at physical locations for care, and those who do not," explained Luber. "There is a growing number of people who are looking for care in non-traditional locations like urgent care centers, at-home, in-dorms, or in other remote locations, which is where binx health can step in."

> When we think about how people consume healthcare, there are essentially two kinds of populations – those who show up at physical locations for care, and those who do not. There is a growing number of people who are looking for care in non-traditional locations like urgent care centers, at-home, in-dorms, or in other remote locations, which is where binx health can step in.
>
> **– Jeff Luber, CEO, binx health, inc.**

The diagnostics arena has proven how powerful the combination of clinical data and powerful new technologies can be.

**The next generation of drug delivery**

As pharma and biopharma companies advance their pipelines to meet a range of unmet medical needs, certain new molecules require novel methods of delivery. Crucial to their success is the work of companies specializing in alternative drug delivery methods that work with innovators who have invested hundreds of millions of dollars on the API side to get over the finish line in safely and effectively reaching patients.

Dyve Biosciences is working on a new approach to transdermal drug delivery that dramatically increases the breadth of molecules that can be delivered through the skin to help bridge the gap between drug innovation and implementation. "Innovation within biotech is exciting, but many new APIs and targets being validated will ultimately run into either a delivery challenge that prevents their promotion from preclinical studies into the clinic, or an opportunity to be more effective if delivered in a different way. As drug development addresses more complex biological challenges, increased delivery challenges arise," explained Ryan Beal, the company's CEO.

Beal is most excited about the potential his company's technology has to transform cancer treatment. Its transdermal approach can influence the acidity of the tumor microenvironment in a manner that is impossible with orally dosed drugs and is currently difficult to inject.







# Alec Ford

CEO
**KARIUS**

**What are the most exciting advancements of Karius over the past few years?**

We have improved our Karius Test offerings, and whereas we used to have a few dozen hospitals ordering from us, we now have hundreds of hospitals that have used the test. In 2022 we will probably achieve one of the most important milestones in Karius' history, which will be the readout of a prospective study called PICKUP —an observational trial designed to examine the efficacy of the Karius Test in immunocompromised patients with pneumonia. To put this in context, there are over 600,000 cancer-related deaths in the US each year. Up to half of those are from infection, with pneumonia being the main infection. People get very excited about new therapeutics and diagnostics to screen for cancer, but one of the top threats to a cancer patient today is not a malignancy, but an infection. The application of the Karius Test in this way has monumental implications.

We also have another trial in immunocompromised patients with invasive fungal infections, which have some of the highest mortality rates and are very difficult to diagnose and treat. Finally, we have another data set coming out in 2022 relative to both adult and pediatric patients undergoing stem cell transplantation and diagnosing critical infections.

**What are the advantages of having a diagnostics test based on microbial cell-free DNA?**

The unique advantage of our liquid biopsy test is that it does not require an invasive sample collection of infected tissue or fluid. Instead, it detects small fragments of DNA from the pathogen causing the infection within the bloodstream. In this way, we can find over 1,000 different pathogens from the site of the infection, irrespective of where the infection is in the body.

A second advantage of our test, as evidenced by the clinical validation data, is its ability to often identify the underlying causes of more infections compared to standard of care. We can identify the likely pathogen causing infection typically within 24 hours of receiving the sample. ■

# Yossi Pollak

Co-Founder & CEO
**SIGHT DIAGNOSTICS**

**Can you introduce our readers to Sight Diagnostics?**

We created Sight Diagnostics with the mission to change the blood testing process. We wanted to provide a fast, simple, and accurate diagnostics tool in a compact platform that could be used in a wide range of clinical settings. To do this, we created technology that digitizes blood sampling, essentially replacing the human eye behind the microscope.

Previously, blood samples had to be outsourced because complete blood counts (CBCs) would typically be done in central labs. With Sight OLO, it is now possible to receive lab-grade CBC results in minutes, allowing for faster treatment initiation. Additionally, Sight OLO only requires two drops of blood from a finger prick or venous sample, making it easier to use.

We soon recognized that the ability to digitize blood samples and collect large amounts of blood morphology data could have a far greater impact than just CBCs, so we started to collaborate with pharma companies to develop companion diagnostics capabilities, providing them with tailored tools to streamline the clinical trial process for the development of new drugs.

**How does your technology differ from previous blood tests?**

We stain the cells with a patented combination of dyes or reagents before using different light exposures to collect multispectral images in real-time to count cells and identify anomalies. The process amasses six gigabytes of information in the form of images per sample. Sight Diagnostics has already accumulated over a petabyte of image data from blood samples and, as we continue to expand the database it helps train our AI algorithm to improve its diagnostic performance and develop new capabilities with pharma companies. During our clinical studies at Boston Children's Hospital and Columbia University Hospital in New York, we compared our system to the best-in-class flow cytometry technology and showed the FDA that our testing provides equivalent quality results. ■

Taking an alternative approach, Rani Therapeutics is a clinical-stage biotech company that has come up with a way to turn injectable biologics into pills. The perennial challenge of biologics is overcoming the problem of the gut breaking down these biological materials before they are absorbed effectively. As the biologics industry has exploded in recent years, more patients have had to endure chronic injectable therapies. Rani Therapeutics saw the need for an alternative and developed its RaniPill, a pill that serves as a swallowable auto-injector, bypassing these historic challenges.

According to Talat Imran, the company's CEO, there has been considerable commercial interest in the RaniPill. His company commissioned market research that surveyed US-based patients who take injectable drugs to quantify the interest. "For one group, 76% of 103 participants surveyed indicated they would prefer to take a pill every day than have an injection every six months. And across all groups surveyed in the 611-patient study, participants would prefer a daily pill over their existing injectable treatment regimen," said Imran. "People in general have a clear aversion for needles, so any chronically dosed biologic presents an opportunity for Rani."

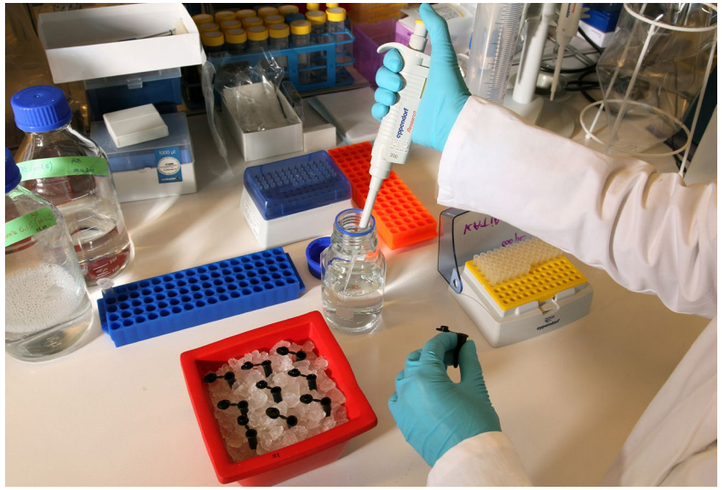


Image courtesy of AC Immune.

In addition to overcoming challenges of how molecules can effectively reach patients, advancements within the drug delivery space have the potential to overcome a significant challenge across therapeutic treatments: medication non-adherence. "Even easy-to-use medicines have measured real-world adherence rates no greater than 50-60% across most chronic diseases," said Adam Mendelsohn, CEO and chairman of Nano Precision Medical (NPM). "Adherence rates in clinical trials are artificially high, and despite how effective available medicines are, the primary reason people do not experience better health outcomes is because they do not take them."

NPM is developing highly miniaturized implants that can maintain constant rate delivery, relieving patients of the burden of daily oral and weekly injectable medicines. The company is particularly focused on metabolic diseases. According to Mendelsohn, within the US alone it has been measured that there are avoidable expenses of approximately US$5,500 per non-adherent patient per year when it comes to type 2 diabetes. Across all diseases, estimates of avoidable expenses that result from medication non-adherence reach US$100-290 billion per year.

From boosting efficacy to ensuring adherence, innovative drug delivery companies provide the crucial link needed to ensure molecules are reaching their full therapeutic potential. ■







> I believe that in the near future we will be able to effectively control the Covid-19 virus with therapeutics.

# James Sapirstein

Chairman, President and CEO
**FIRST WAVE BIOPHARMA**

**How did First Wave BioPharma (First Wave) perform over the past year?**
During the pandemic AzurRx BioPharma decided to acquire First Wave Bio, and the merged company was renamed First Wave BioPharma. Through the transaction and merger, we purchased full rights to First Wave's proprietary formulations of niclosamide and exclusive international rights to develop oral and topical formulations of the compound for all gastrointestinal indications (GI), including Covid-related GI infections; IBD indications including ulcerative colitis (UC) and Crohn's disease; and immune checkpoint inhibitor-associated colitis and diarrhea. We own the method of usage and delivery of these formulations as therapies for several auto-immune, inflammatory and viral ailments.

In 2021 we started enrolling patients into our FW-COV trial, involving the delivery of a proprietary oral tablet formulation of micronized niclosamide for the treatment of Covid-19 related GI infections. We believe that vaccines are not the answer to resolving Covid and that therapeutics are necessary to help us get on the other side of the pandemic. Through our trials, we hope to demonstrate the safety of niclosamide in the treatment of patients with Covid 19 GI infection and to prove efficacy in clearing the virus from the GI tract. We have also started advancing our FW-UP study, a niclosamide-based, topical anti-inflammatory inhibitor therapy for the treatment of ulcerative proctitis (UP) and ulcerative proctosigmoiditis (UPS), two forms of ulcerative colitis.

**What can niclosamide do which vaccines cannot?**
Current Covid vaccines work on the spike proteins, which is where the viral mutations, such as Omicron, occur. Our niclosamide formulations are spike-agnostic; they work in the virus membrane and are not dictated by mutations that might happen. Our drug explodes the membrane of the virus so that it cannot replicate. The Covid virus also causes inflammation and niclosamide has anti-inflammatory properties that has been safely used on millions of patients worldwide. I believe that in the near future we will be able to effectively control the Covid virus with therapeutics.

**How far progressed is First Wave's FW-COV study?**
We completed enrollment in the FW-COV study with over 167 patients on 4 January 2022 and are in the process of tabulating the final data. We know that niclosamide does not have an antiviral effect on Covid-19. Unfortunately, the results did not demonstrate efficacy from the virology front, but we are still working through the data to determine it's effect in the GI system. The trial did produce strong safety results which can be utilized in the future development program.

**Can you elaborate on First Wave's second proprietary technology, adrulipase?**
Adrulipase is a recombinant lipase enzyme designed to enable the digestion of fats and other nutrients. First Wave conducted two studies addressing Exocrine Pancreatic Insufficiency (EPI) in patients with cystic fibrosis and chronic pancreatitis, with one study delivering mixed results and the other extremely good results. The patients in our combination study, where we added adrulipase to existing therapy, did really well. In our mono-therapy trial, where we compared ourselves to other PERTs on the market, our drug had great effects in some patients but no effect in others. We immediately started working on a new formulation and are at the end stage of completing laboratory testing and moving on to human patients again. If we can accomplish uniform absorption in humans with the new formulation in the next Phase 2 study, which we anticipate will initiate in the second half of 2022, we can move to a pivotal Phase 3 trial.

**How aggressive is the Intellectual Property (IP) landscape in the U.S.?**
US companies usually have a narrow window to monetize a product under patent. Patents generally last for 20 years from the moment you file for IP, however it typically takes a company 8-12 years to develop a drug and bring it to market. Generic companies will start producing formulations often before the patent expires to be ready to hit the marketplace as soon as the patent restrictions are lifted. First Wave is fortunate to have very strong formulation, method of use, and indication patents for both niclosamide and adrulipase and our key IP is secure for 15-20 years.

**What are First Wave's objectives for the next two years?**
We will continue advancing our pipeline to become a fully developed GI company and hope to get both adrulipase and niclosamide to the market as soon as possible. ■

# Talat Imran

CEO
**RANI THERAPEUTICS**

**Can you introduce our readers to the vision behind Rani Therapeutics?**
Rani Therapeutics is a clinical-stage biotech company that takes injectable biologics and turns them into pills. Rani Therapeutics developed the RaniPill capsule, which functions as a swallowable auto-injector and enables oral delivery of biologics.

The RaniPill capsule has a pH-sensitive protective coating so the capsule passes through the stomach without dissolving and enters into the small intestine where the pH is higher. There, the capsule dissolves and exposes a little plastic bag with a dissolvable pinch valve that separates the bag into two compartments. When the valve dissolves, potassium bicarbonate and citric acid mix to produce carbon dioxide, which serves as the energy source for the robotic pill. The bag then inflates, exerting pressure on a syringe with a hollow, dissolvable microneedle containing a solid tablet of the drug. Once the bag reaches sufficient pressure, the piston inserts the needle into the wall of the small intestine, and because there are no sharp pain receptors in the gut, the patient feels nothing. After injection, the bag deflates and is excreted. The needle dissolves within 10 minutes, and the drug is readily absorbed by the highly vascularized intestinal tissue. This process allows for the delivery of a variety of biologics, including peptides, monoclonal antibodies, and large proteins. ■

# Adam Mendelsohn

CEO, Co-Founder & Chairman
**NANO PRECISION MEDICAL**

**Can you introduce our readers to Nano Precision Medical (NPM) and elaborate on the need you saw in the life sciences space to provide an alternative drug delivery offering?**
Medication non-adherence is a significant problem – even easy-to-use medicines have measured real-world adherence rates no greater than 50-60% across most chronic diseases. Adherence rates in clinical trials are artificially high, and despite how effective available medicines are, the primary reason people do not experience better health outcomes is because they do not take them. This is particularly true with metabolic diseases, where NPM is focusing initially with type 2 diabetes being the first indication we are pursuing.

Our goal is to enable medicines that already exist to achieve their maximum potential by guaranteeing adherence. At first, we are developing a small six-month implant for the treatment of Type 2 Diabetes that can be inserted in an outpatient procedure in just a few minutes. The company also has two feasibility programs in development in the areas of non-alcoholic steatohepatitis (NASH) and obesity. Ultimately, the technology is a platform which we expect will result in a portfolio of drug implants across a variety of disease areas. ■

# Ryan Beal

Co-Founder & CEO
**DYVE BIOSCIENCES**

**What is Dyve Biosciences working on?**
Dyve Biosciences is a clinical-stage biotech company based in Southern California that is pioneering a new approach to transdermal drug delivery. It is breaking down barriers of the breadth of molecules that can be delivered through the skin.

2021 was a big year for us. Internally, we advanced our first program through a successful phase 2. DYV-702 is a study for a topical treatment for acute gouty arthritis, and we are looking forward to continuing development here. We also made two big strides with external collaborations, including one with a top-ten pharmaceutical company that has several targets within their portfolio they are hoping to shift from oral or injectable to transdermal. We are also working with the Moffitt Cancer Center given their interest in our approach of delivering pH-modulating therapies through the skin.

This method allows us to deliver pharmacokinetic profiles that look much more like an injection than you would expect. It also allows us to get a broader range of molecules through the skin, perhaps even 80% of small molecules, and we will focus on advancing therapeutics that have been proven to work but are not able to be delivered with current routes of administration. We see particular use cases in oral drugs that have adverse GI impacts or as replacements to needles. ■





## From the eye to the gut, the following companies are advancing the standard of care for several different therapeutic areas.

"Outlook Therapeutics hopes to bring to market an investigational ophthalmic version of bevacizumab, a molecule that has been used to treat retinal disorders for several years but has never received approval from major regulatory agencies to be used as an ophthalmic drug solution. If our ophthalmic bevacizumab is approved, we will potentially enhance the standard of care for patients with disorders like wet AMD, diabetic macular edema, and branch retinal vein occlusion by removing concerns related to off-label repackaged IV product. We firmly believe that if a substance is to be injected into a patient's eye, it should meet the various requirements necessary to earn FDA approval for ophthalmic use."

**– Russell Trenary, President & CEO, Outlook Therapeutics**

"Our mission is to bring novel and transformative therapies to the anterior (front) chamber of the eye, particularly for the treatment of ocular surface disease. The company obtained its first FDA approval in 2021 for its Tyrvaya medication, the first and only nasal spray for the treatment of the signs and symptoms of dry eye disease."

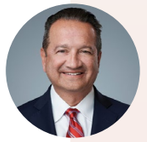
**– Jeffrey Nau, President & CEO, Oyster Point Pharma**

"The company's second pillar, brensocatib, is currently in a phase 3 clinical trial as the first investigational DPP1 inhibitor developed for neutrophil-driven inflammatory conditions... The drug is unique in that it targets the inflammatory process associated with bronchiectasis rather than the historically unsuccessful approach of treating with anti-infectives. Results from the phase 2 trial were published in the New England Journal of Medicine, the first time in nearly 20 years this journal has published on bronchiectasis."

**– Will Lewis, Chairman & CEO, Insmed**

"We are developing product candidates of standardized composition based on defined bacterial strains grown from clonal cell banks in a manner analogous to monoclonal antibody production... We believe that our targeted approach could offer consistent composition and quality attributes, provide more consistent clinical benefit, limit safety risk, and enable scalability compared with fecal-derived approaches."

**– Bernat Olle, CEO, Vedanta Biosciences**



"During the pandemic AzurRx BioPharma decided to acquire First Wave Bio, and the merged company was renamed First Wave BioPharma. Through the transaction and merger, we purchased full rights to First Wave's proprietary formulations of niclosamide and exclusive international rights to develop oral and topical formulations of the compound for all gastrointestinal indications including Covid-related GI infections, IBD indications including ulcerative colitis (UC) and Crohn's disease, and immune checkpoint inhibitor-associated colitis and diarrhea. We own the method of usage and delivery of these formulations as therapies for several auto-immune, inflammatory and viral ailments."

**– James Sapirstein, Chairman, President and CEO, First Wave BioPharma**


# CONTRACT MANUFACTURING AND CHEMICALS

"Our customers have long vocalized a preference for Western-based CDMOs. This has increased over the last few years as Covid-19 and recent geopolitical events have revealed the vulnerability of global supply chains."

**– Thomas Loewald,**
**CEO,**
**Cambrex**



Image courtesy of AMPAC Fine Chemicals, an SK pharmteco Company

# A Shifting Landscape

## The outsourcing model is here to stay

Outsourced manufacturing and development companies have responded to the increased demand for their services in full force, evolving into true partners that play a critical role within the life sciences ecosystem.

In general, demand for CDMO services continues to grow. Research and Markets predicts the global pharmaceutical API manufacturing market will expand from US$195 billion in 2022 to over US$250 billion by 2026. This can be attributed in part to life sciences companies resuming their operations, some scientists putting their lab coats back on for the first time in nearly two years.

A more deep-rooted shift, however, is largely responsible for this uptick in demand, one that has been unfolding in the drug discovery space for the past several years: it is no longer the biggest players in pharma who claim ownership to the development pipeline and the commercialization of new drugs. Increasingly, small and mid-size companies, primarily biopharma and biotech, require support to advance their molecules. These companies often receive ample funding to develop their pipelines without having the in-house manufacturing capabilities to do so alone.

Jonathan Hunt, managing director and CEO of Syngene International, an integrated research, development and manufacturing organization noted: "Five years ago, our stereotypical customer was a big pharma company that utilized our services for one aspect of their molecule's lifecycle, whereas today our customer base is filled more with young start-up biotech companies that have small leadership teams and no infrastructure but are well funded."

This shift does not just lead to more work, but also to a more engaged, collaborative environment. According to Hunt: "They are looking for more than just hands to do work; they value the scientific insights, scale and technology we bring to their projects."

The rise of small companies with stripped-down capabilities, some so spartan as to be called "virtual pharma," mean the contract manufacturing model will remain a vital organ for the overall health of the industry.

### Standing out in a saturated environment

The heightened attention contract development and manufacturing companies are receiving has forced players in the space to strengthen their competitive edge in order to stay relevant.

One solution has been to work on increasing the speed with which clients can use services to progress their molecules to market. In the life sciences industry speed is paramount; patents remain valid 20 years past the filing date, yet it takes the average company at least a decade to get a product to market. Any time saved in the process – whether it be three months or one year – is time added to that patent clock, which not only increases the period of economic value for the company but also accelerates treatment for patient populations in need.

For the past few years, Lonza's mammalian biopharmaceutical branch has been working on accelerating its clients' pipelines through its Ibex Design offering. Jennifer Cannon, the SVP global head of mammalian biologics at the company, acknowledged: "We see in the market that many clients are investing in the development of bioconjugates. As such, the market seeks faster, more reliable and simplified supply chains to support the development and commercialization of new bioconjugate molecules."

Ibex Design, which leverages technologies, tech transfer capabilities, and automated bioprocesses, claimed to meet three significant milestones for clients: 5 months from DNA to TOX drug substance; 11 months from DNA to IND/IMPD; and minimum 1.5 kg GMP drug substance for phase 1 clinical trials. The company also invested in a drug product vial filling facility to complement its antibody-drug conjugate facility. "Together, this offers a one-stop-shop experience to our clients, which simplifies the supply chain, de-risks technical exchange of materials and data, and facilitates program management," explained Cannon.

In addition to speed, clients also want ease. Rather than working with several service providers along a product's lifecycle, for example, it is much easier to work with just a few. To streamline the drug development process, Quotient Sciences' CEO Mark Egerton sees value in CDMOs managing both drug substance and drug product in parallel. "Previously, customers would use service providers upstream from us and make decisions on which compounds to progress without much consideration of what would happen downstream," explained Egerton. "The customer would sometimes manufacture the drug substance only to find out later they had made an error in the compound selection process. Having already made significant investment, they are reluctant to take a step back and thus start to make compromises for their downstream development plan."

Instead, Egerton believes his company's involvement in the development process from the moment in which a drug molecule is selected from the discovery program reduces such complications down the line and allows for a more streamlined workflow.

### Specialized technology drives the day

While more streamlined, one-stop-shop business models entice clients with heightened speed and facility throughout the outsourcing process, the true differentiator in a bustling service provider environment is investment into specialized technology that can suit clients' ever-complexifying demands.

As Jan Kengelbach, CEO of Aenova Group sees it, competition on older lifecycle products is exacerbated by the relevance of Asian competitors. Since assuming the role of CEO, he has taken the company down a different route – focusing instead on tapping into more strategic and technologically advanced manufacturing of drug products. "It is imperative to have a technological edge," Kengelbach commented.

Aenova was already a leader in the European market for solid dosage forms, but he decided to investigate unique technologies the company could provide to further differentiate itself in the space. "If a customer might have a more complicated request, like a multi-unit pellet system, we can provide the appropriate level of scientific expertise and cutting-edge process technology such that the client immediately trusts they have found a reliable counterpart," Kengelbach explained. "Recently, we won a project on highly innovative intra-oral implants, something that is not obvious to do in solid dose manufacturing. We got this contract because of our upfront investments in the right scientific and technological expertise."

As the CDMO space is becoming more competitive, finding the right balance between cutting-edge technology and scalable, cost-effective manufacturing practices will be imperative for success. ■

> The growth in large molecules has been extremely impressive, and we are tapping into this market.

# Thomas Loewald

CEO
**CAMBREX**

**Could you provide an overview of Cambrex's core services?**
Cambrex is a global CDMO that provides drug substance, drug product, and analytical services across the entire drug lifecycle, helping our customers develop and deliver life-improving therapeutics. In 2021, we celebrated our 40th year with a growing team of over 2,200 employees serving global clients from 12 facilities across North America and Europe.

Cambrex offers clients the ability to work with us from the preclinical stage through the product lifecycle into commercialization. For drug substance we offer a range of technology enabling us to serve most small molecules, including continuous flow, biocatalysis, controlled substances, highly potent products, and a range of production scales from kilo labs to 16,000 liters. We offer a wide range of dosage forms including tablets, capsules, extended-release formulations, liquids, semi-solids, suppositories and pediatric formulations.

**How important are small molecule and large molecule therapeutics to Cambrex?**
Historically, our core business has been developing and manufacturing small molecule therapeutics. Small and mid-size biotech and pharma companies are leading the way, owning a growing share of the development pipeline compared to their big pharma peers. Additionally, orphan drug approvals account for an increasing proportion of new approvals. We have invested over US$100 million in capacity expansion across clinical and commercial production to meet demand.

Newer to Cambrex is the large molecule space, where we have a rapidly growing analytical business serving biopharmaceutical products and have invested in labs, equipment and talent to support increasing demand. The large molecule market is growing at an even faster rate than the small molecule side, and we see strong demand for analytical services supporting the development and manufacturing of biopharmaceutical products. It was a natural step for us to serve biotherapeutics as we were driven by previous customers requesting we broaden our range of analytical services. We also saw significant overlap in the instrumentation used to support small molecules.

**How does Cambrex's "reverse engineering methodology" in drug development ensure on-time product delivery amid supply chain disruptions?**
Using the reverse engineering approach our teams plan projects from the end to the beginning by looking for critical path materials or activities, proactively moving those items off the critical path, then repeating. While this does not make Cambrex completely immune to supply chain disruptions, it ensures the company has the most robust project plan possible before the first raw materials are ordered.

**What key trends do you see presently driving the life sciences space, and how do these inform your business strategy?**
The first trend is the ownership of the development pipeline and commercialization of new products shifting from large pharma to small and mid-size companies. This has driven an increased level of outsourcing, as smaller companies tend to need more support along the development journey and often own no commercial-scale manufacturing assets. CDMO outsourcing rates are still relatively low, roughly 40-50% depending on the service, and we expect that rate to continue to grow.

The second trend is the emergence of more targeted, personalized medicine with orphan drug approvals now exceeding non-orphan drug approvals. This has two impacts on our business. First, we need more flexible manufacturing assets to support a wide range of batch sizes and the technologies to cover the development of those molecules. For this reason, we are investing in small-scale commercial assets and highly potent technology at our High Point, NC facility. Second, smaller batch sizes lead to a higher level of demand for analytical resources relative to manufacturing assets, as each batch must be tested the same way, whether it is enough material to treat 10 patients or 10,000 patients. We have seen an industry-wide shortage in analytical resources, creating a very strong demand in our analytical service portfolio.

Finally, we have seen robust growth across small and large molecules, but higher growth in new modalities such as cell and gene therapy. The growth in large molecules has been extremely impressive, and we are tapping into this market.

**What is Cambrex's business development strategy for the next few years?**
Cambrex has a track record of above-market growth over the past 10 years, and our goal is to continue that trend. We have great organic growth opportunities and will continue to invest heavily in our core business. On the inorganic side, our priorities include adding scale to our core business, complementary technologies that would allow us to serve a broader cross-section of our customers' pipelines, and potentially new services that would increase our exposure to the large molecule market. ■





> Syngene is currently piloting a relay-based drug discovery cycle utilizing all 24 hours in the day that we estimate reduces early discovery timelines by 12 to 18 months.

# Jonathan Hunt

Managing Director and CEO
**SYNGENE INTERNATIONAL**

**What are Syngene's core services?**
Syngene's operations are divided into four divisions. Within the R&D space, we have our Discovery Services and Dedicated Centers, which remain at the core of our operations. Additionally, we focus on scaling up our offerings in Development and Manufacturing services. Over the past decades, we have become increasingly like our clients by integrating our services so we can act as a scientific equal and collaborator and have worked on becoming a platform for integrated drug discovery that allows us to partner with players of all sizes. Five years ago, our stereotypical customer was a big pharma company that utilized our services for one aspect of their molecule's lifecycle, whereas today our customer base is filled more with young start-up biotech companies that have small leadership teams and no infrastructure but are well funded. They are looking for more than just hands to do work; they value the scientific insights, scale, and technology we bring to their projects.

**Can you elaborate on the rationale behind SynVantage, the company's relay-based drug discovery process?**
The primary economic asset in this industry is a patent, something that by nature decreases in value on a linear basis. Patents are typically for 20 years, and once patented it takes a molecule an average of 10-12 years to reach the market. This means the patent-holding company experiences an approximate eight-year return. I have always felt drug discovery and the Design-Make-Test-Analyze cycle should be amenable to process flow execution, such that we can significantly minimize the amount of time required drive a program through to candidate selection, and hence to the IND, both key milestones along the way to eventual product launch. If you can achieve in twelve months what typically takes twenty-four months, you have successfully added twelve months to the patent clock, thereby meaningfully increasing the period of economic value. This could lead to millions more in profit as well as improve lives for patient populations. Syngene is currently piloting a relay-based drug discovery cycle utilizing all 24 hours in the day that we estimate reduces early discovery timelines by 12 to 18 months.

**How would you rate the current degree of collaboration within the life sciences?**
The degree of collaboration within life sciences has been unprecedented, including academia, governments and regulators, and industry participants like pharma, biotech, and service companies. When we write this bit of history, it will remain astounding that we have not one, but multiple Covid-19 vaccines, and that millions of people have been vaccinated. Just two years ago, even industry insiders would have found this hard to believe.

In the US there is a perception that pharma companies are overly profit-driven, yet industry members have proven the exact opposite. For example, AstraZeneca was not in the vaccine business at the onset of the pandemic, but the executive team decided to throw resources into developing a vaccine in a largely not-for-profit manner, understanding the global need. This is about as altruistic as a public company can be.

**How important is the US to Syngene's global operations?**
The US market is the largest life sciences market and is strategically important for us, home to over 70% of our customers. Two of our most important relationships are with US pharma giants, BMS and Amgen, for whom we run dedicated research facilities in Bangalore. That said, pharmaceutical science does not happen on a national level. My immediate client may be a US company, but it is likely to have global scientific research teams.

**What does the future hold for Syngene?**
Syngene is well-positioned to meet our clients' evolving requirements and capture market opportunities as they arise. In particular, Syngene has invested in expanding its biologics manufacturing and commercial manufacturing of APIs. The growing demand for outsourced biologics manufacturing and encouraging growth in the biologics business has encouraged us to continue building our capacity year-on-year. The API facility will strengthen our position as a one-stop solution provider across discovery, development and manufacturing. The facility has been designed as a state of the art, small molecule manufacturing facility to deliver NCEs and niche generics.

We expect to see these investments contributing to top-line growth of the company, taking Syngene from having two to four business drivers while establishing a balanced portfolio between the research and manufacturing sides of the business. ■

> Our reputation is based on how we deploy technologies to solve complex formulation challenges.

# Tom Sellig

CEO
**ADARE PHARMA SOLUTIONS**

**Can you share highlights of Adare's operations over the past year?**
Our acquisition of Frontida BioPharm in 2021 afforded us some new capabilities that are complementary and synergistic to what Adare already had. We now have high-potency capabilities, our packaging facility in Northeast Philadelphia, and several other exciting technologies, scientists, and formulators. Our focus this year has been on integrating the leadership team and establishing our strategic plan moving forward.

**How has the Frontida acquisition expanded the company's offerings?**
With the Frontida consolidation, our expanded market presence heightens our ability to offer more solutions to more customers. Consequently, we are currently working on a pipeline of 75 development products, which represents an exciting growth opportunity for the company.

The acquisition enabled tremendous expansion in three core dimensions: capabilities, capacity and expertise. We now have additional DEA capabilities across multiple sites for development and manufacturing, as well as packaging capabilities, allowing us to phase out third-party packaging for several legacy products. Regarding capacity, we have added three new sites to our network, enabling us to expand our geographic footprint and actual output both in development and manufacturing capacities. Finally, our scientific team has increased to a combined 100 world-class developers and scientists.

**Does Adare leverage any innovative technologies?**
Adare's foundation is built on our long legacy of innovative technology. We are industry-leading experts in several technologies used in development and commercial manufacturing, such as microencapsulation, taste masking, controlled release, and multilayer tableting. Combined with Frontida's high-potency capabilities, we offer a comprehensive range of oral solid and small molecule solutions. Our market reputation is based on how we deploy these technologies to solve complex formulation challenges, and we've become known for taking on these challenges and providing customized solutions for our customers.

**What does Adare Biome add to the company's portfolio?**
The division works to harness the power of the microbiome to provide post-biotic solutions for human and animal health. Biome-based products are present in everything from human pharma and OTC products to nutritional supplements. The emerging utility of this type of product encompasses different market segments in the pharma space, including oncology, respiratory, and a variety of CNS-related products. We are excited about the potential future for biome-based products.

**How has Adare responded to Covid-related challenges?**
Our global supply chain team was very proactive and monitored the various APIs and materials that we use in our manufacturing and packaging capabilities, and they managed to limit the level of disruption to rare instances. In some cases, we have capitalized on our existing inventory and capacity to pivot quickly to meet pressing client demands while satisfying regulatory lead times for product approval.

On the resourcing and staffing front, our human resources team had to get creative to maintain a high level of retention and keep some of the market leaders.

**Could you provide an overview of Adare's US operations?**
Adare is a US company headquartered in Lawrenceville, New Jersey. In the US, we also have five manufacturing and development sites. Two are located in Philadelphia, Pennsylvania, and the other three are in Vandalia, Ohio; Aurora, Illinois; and Lenexa, Kansas.

Adare is an international company that distributes and markets products in over 100 countries worldwide. Internationally, we have two sites with development and commercial manufacturing capabilities in Milan, Italy, and a post-biotic plant in Houdan, France. While each site is unique, there are certain crossover capabilities where we can perform business continuity and supply chain backup for our clients to prevent supply chain disruptions.

**Has Adare been impacted by the trend towards increasing domestic drug manufacturing in the US?**
This trend, which is largely triggered by the rising cost of transportation and inflation, has benefitted Adare. The company recently had six clients in one week alone reach out to move a large portion of their US production onshore. We are well positioned to facilitate moves like this by aligning clients with the right US manufacturer. Thus, we have the capacity to support an increase in business from the growing trend.

**What are your growth plans for Adare for 2022 and the coming years?**
We intend to accelerate our ability to meet client needs and provide excellent customer service as we transition from a product-based to service-based company. Moreover, we aim to leverage our specialized technologies and experienced staff to drive organizational growth. Finally, we want to emerge as an industry leader in the biome space. ■





> While it´s always easier to deny a certain service if you don't yet have the technical expertise in a particular area, in the long-term it is advantageous to explore the possibility of investing in that area with the customer.

# Jan Kengelbach

CEO
**AENOVA GROUP**

**Can you introduce our readers to core operations of Aenova Group (Aenova)?**
Aenova is one of the largest CDMOs worldwide, with US$700 million sales, spanning the entire dosage form spectrum and nearly all therapeutic areas. We are organized in three business units: solids, semi-solids, and liquids, offering end-to-end services from new chemical entity discovery through clinical phase management to market release. We have 500 customers and operate out of 14 sites in Europe and one in the US.

**What are the main strategic positionings of CDMOs in today's life sciences industry?**
Within the CDMO space, there are a few options for how to strategically position yourself. Historically, the majority come from a more CMO-oriented place, in which you are basically an extended capacity provider for products older in the lifecycle. To do well going this route, you must understand optimizing efficiencies and economies of scale. The competition on older lifecycle products is more pronounced. If you want to participate in the strategic and cutting-edge manufacturing of drug products, however, you need strong development and tech transfer services.

Additionally, it depends on the type of customers and products you want to attract. Bigger pharmaceutical companies have their own development teams but may still need a manufacturing and development partner to bring their product to market. Leaner players often pursue an asset-light model with virtually no manufacturing footprint and are dependent on a fully integrated development service provided by their CDMO partner. As such, which strategic approach you take to the market and where you want to play determines the services you must provide.

**How important is innovative technology for CDMOs to stand out from their competition?**
It is imperative to have a technological edge. Aenova was already the top CDMO for solid dosage forms in Europe, but we thought critically about what unique technologies we could provide at our 12 sites with solid dosage form capabilities to distinguish from the competition. If a customer might have a more complicated request, like a multi-unit pellet system, we can provide the appropriate level of scientific expertise and cutting-edge process technology such that the client immediately trusts they have found a reliable counterpart. Recently, we won a project on highly innovative intra-oral implants, something that is not obvious to do in solid dose manufacturing. We got this contract because of our upfront investments in the right scientific and technological expertise.

**Can you elaborate on the technologies Aenova currently offers its clients and how it decides what new technologies to invest in?**
Recently, Aenova has focused on bringing in new, differentiating technologies. None of these are new to humankind, but for many it is the first time they are offered on a CDMO platform of our size. Many are related to enhanced bioavailability of the drugs. We have several projects in our high potency area, particularly in oncology, where we take injectable drugs and try to convert them into solids by applying innovative technology and drug formulation concepts. We also offer sophisticated over-encapsulations, in which we can put an immediate and sustained release tablet in a capsule to design the therapeutic effect of different molecules. Aenova has also built a dry powder inhaler platform and can make micro-dosed filling comprised of tiny quantities of the API down to the microgram. As the second largest softgel capsule player worldwide, we see increased demand for microcapsules, softgel capsules the size of the head of a needle. These are only few examples of innovative technologies Aenova can offer its clients.

With these technologies, the company has gained access to a new set of customers willing to co-invest in these projects with us. The problem with many large-scale providers is they do primarily older lifecycle products, but we are clearly committed to bringing newer lifecycle products to life. We remain open to requests that require an update to our current capabilities. While it´s always easier to deny a certain service if you don't yet have the technical expertise in a particular area, in the long-term it is advantageous to explore the possibility of investing in that area with the customer. This is the partnership approach and the change in mentality we successfully implement. The minute you have your first proof of concept, more requests will come quickly and you are off to building a new growth platform. ■

## Robert Lee

President of CDMO Division
LUBRIZOL LIFE SCIENCE

**Can you provide an overview of Lubrizol's CDMO Division?**
Lubrizol is a full-service CDMO that grew out of the drug delivery space, which continues to be our core competence. We offer all supporting services including analytical method development and validation, physicochemical characterization, and manufacturing of drug products for R&D through cGMP. Our versatility allows us to handle highly potent compounds along with DEA controlled drugs from schedules 1 through 5. Lubrizol covers virtually every route of administration with 60% of our programs being parenteral, 25% ophthalmic, and the rest divided between topical, mucosal, and oral.

Around 35% of our programs are new chemical entities under NDAs, 35% 505(b)(2) applications, and the rest is split between ANDAs and OTCs. Our clients range from venture-base startups to the largest pharma, generic, biotech companies and everything in between. As a result, we work with a variety of molecules – around 85% being small molecules and the rest biologics.

**Which services did you see the most demand for in 2021?**
Lubrizol has been working on many ophthalmic projects in both the topical and intravitreal space as well as proprietary PLGA microparticles for intravitreal administration. We have a very robust drug-eluting device group which is designing and manufacturing intraocular implants, something we recently signed a program to do the commercial manufacturing for. We are also seeing a lot of interesting dosage forms, including quite a bit of nasal delivery and nanomilling, which remains a key option for formulating water-insoluble compounds.

**What is Lubrizol's vision for its CDMO division over the next few years?**
Lubrizol will focus on its commercial manufacturing, as we have the capabilities to take development projects into GMP production. We believe the demand for sterile and aseptic manufacturing services will continue to increase, given the growth in biologics and their integration into drug/device combination products. Additionally as many nano- and microparticulate-based formulations are not amenable to terminal sterilization, we see aseptic nanomilling as a great option because it supports every sterile route of administration. ■

## Jennifer Cannon

SVP Global Head of
Mammalian Biologics
LONZA

**What is driving the mammalian cell culture space in 2022, and which of the company's services are most in demand?**
Lonza's strength and expertise over the past 35 years has been based on the company's capabilities around cell culture development in clinical and commercial manufacturing. We continue to strengthen our offerings by further developing and expanding our host cell lines, improving our manufacturing platform, and investing in our tech transfer capabilities. Much of our R&D efforts are focused on increasing titers and improving the stability of constructed cell lines. This not only ensures better commercial viability of molecules but also helps Lonza clients to understand what flexibility and improvements to cost of goods they may benefit from long term.

**Can you highlight key initiatives Lonza has been involved in over the past year?**
An initiative that we embarked upon before the pandemic is our Ibex Design offering. Ibex Design leverages Lonza's technologies, tech transfer capabilities, and automated bioprocesses to meet the huge surge in interest in speed to clinic. Our fixed-price, fastest DNA-to-IND program is packaged in a standardized platform to allow clients to bring a new antibody molecule to IND filing in a rapid amount of time, guaranteeing to break through three major milestones: 5 months from DNA to TOX drug substance; 11 months from DNA to IND/IMPD; and minimum 1.5 kg GMP drug substance for phase 1 clinical trials.

This initiative leverages our versatile cell line engineering technology called GS piggyBac. This platform allows us to deliver higher titers and a more robust and reliable output of complex proteins and monoclonal antibodies. In turn, our clients will see improved cost of goods in the long term as their molecules proceed through the clinic.

Finally, we have added capabilities and capacity at four of our sites, including our facilities in Switzerland, China, UK and Singapore to facilitate speed to clinic and support the development of increasingly complex novel biotherapeutics. ■





# Keeping up with Demands

## CDMOs diversify their capabilities to meet their clients' complex requirements

Image courtesy of CordenPharma.

Just as the change in profile of the average customer seeking out a manufacturing partner has led to a restructuring of the CMO / CDMO landscape, evolution in the types of projects pharma and biopharma companies decide to take on impacts the services their contract counterparts invest in.

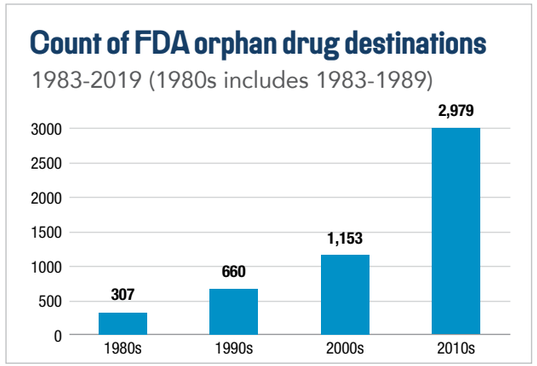
**The smaller the patient populations, the bigger the push for CDMOs**
To accommodate the rise of programs using targeted medicines to treat rare disorders, many CDMOs have restructured their supply chains accordingly.

The Orphan Drug Act of 1983 has played an immense role in the attention orphan products now receive. Before its enactment, only 38 orphan drugs existed; between 1983 and July 2020, the FDA approved 599 drugs for the treatment of rare diseases. In fact, throughout the past five years, roughly half of all drugs approved by the FDA have been for orphan or rare disease indications.

Shuang Liu, CEO and founder of ConSynance Therapeutics, a clinical-stage virtual biopharmaceutical company focusing on rare diseases in the central nervous system, sees clear benefits to operating within the US beyond its regulatory appeal: "The US is the leading country for rare disease research thanks to its patient-centric ecosystem fostered by the government, patient advocacy groups, industry, research institutions, and the general regulatory environment. The US has the most favorable environment for rare disease research given the ability to take on high-risk endeavors that have the potential to transform the treatment of rare disease patients and significantly improve their quality of life."

The capital inflow into the space has enabled companies with ambitious programs to fund research into diseases that can be so rare they are not even registered within the FDA, much less have a preexisting approved treatment. The market for these drugs is inherently smaller, sometimes in the mere thousands, which has flipped the traditional development and manufacturing model on its head, a far cry from blockbuster drugs that are designed to reach millions of patients.

One of the most fundamental ways service providers have accommodated to working on smaller batches is in the way they approach supply chains. According to Mark Egerton of Quotient Sciences, pharmaceutical companies developing drugs to treat rare disorders have two options in terms of distribution. They can either invest substantially into producing large quantities of product with an extended shelf life or hold off until patients have already been recruited and then deliver the drug to this population in a near just-in-time fashion. The latter is often attractive when dealing with patient populations so small that the recruitment process for




Source: Orphanet Journal of Rare Diseases

trials can be a long and unpredictable journey.

Thomas Loewald, CEO of Cambrex, drew two conclusions from the fact that the number of orphan drug approvals currently exceeds non-orphan drug approvals: First, his company needed to establish more flexible manufacturing assets to accommodate a greater variety in batch sizes and the technologies to assist with the development of the molecules in question. Second, projects for more targeted medicines require greater analytical capabilities. "Smaller batch sizes lead to a higher level of demand for analytical resources relative to manufacturing, as each batch must be tested the same way, whether it is enough material to treat 10 patients or 10,000 patients," Loewald explained. "We have seen an industry-wide shortage in analytical resources, creating a very strong demand in our analytical service portfolio."

In addition to generating a stronger focus on supply chain flexibility, the heightened interest in treating rare disorders has itself driven more demand for outsourcing to service providers. As Patricio Massera, CEO of AGC Biologics commented, smaller production volumes make it more difficult for small and mid-sized developers to find value in establishing their own manufacturing capacity. "CDMOs offer a great opportunity for orphan drug developers to outsource manufacturing capabilities so they can focus on the science and strategic planning to get their products to the market," he explained.

**Going green**

Over the past handful of years, rising ESG concerns have made their mark within nearly all major industries. Life sciences is no different.

Customers of service providers are demanding more environmentally conscious manufacturing methods and sustainably sourced products, and the requirement is not unfounded. According to the European Environmental Bureau, more than 100,000 tons of pharmaceutical products are consumed annually around the world. Throughout their manufacture, consumption, and ultimately disposal, chemical ingredients are released into the surrounding environment. It is estimated that between 30-90% of the APIs in an oral dose are excreted as urine. As these products are designed with the express purpose of causing pharmacological effects in living organisms, their release into the broader ecosystem can lead to unintended consequences.

Industry agnostic concerns such as carbon footprint are also ever-present; it has been widely reported that the pharma sector historically generates more greenhouse gases than the automotive industry. Broadly adopted initiatives to shorten and strategically reshuffle supply chains will likely mitigate the problem, but some CDMOs believe that is not enough. Green chemistry aims to reduce pollution at the source by minimizing or eliminating altogether the environmental risks posed by chemical feedstocks and products.

The European Environmental Bureau estimates that only 1% of all input materials end up in a drug substance, meaning that taking heed to select the most important chemicals is a win-win for companies: they can simultaneously lessen their impact on the environment and save money by using fewer materials. For Murli Krishna Pharma Pvt Ltd, an Indian-based drug delivery system company, the selection process for polymers is paramount. "We take pride in developing formulations with thoughtful selection of matrix and cogent selection of polymers," said Satya Vadlamani, the company's chairperson and managing director. "We select the matrix based on the physico-chemical properties of the drug molecule and develop products using an aqueous base instead of organic solvents to avoid toxic effects that might arise from organic solvents."

Michael Quirmbach, CEO and president of global CDMO CordenPharma, highlighted how his company focuses on mitigating its environmental footprint: "Green chemistry entails the methods we employ to reduce the use of certain organic solvents and how we run our processes more volume-efficiently than in the past," he explained.

CordenPharma has partnered with PeptiSystems, a Swedish-based developer of instruments for peptide and oligonucleotide therapeutic process development and manufacturing, to reduce the waste inherent in peptide production. According to Quirmbach, PeptiSystems has developed a continuous manufacturing process that reduces solvent consumption and waste by at least 40%.

For Trevor P. Castor, president and CEO of Aphios Corporation, a company specialized in developing green, enabling biotechnology and nanotechnology drug delivery platforms, finding alternatives to the traditional pharmaceutical business model that generates large amounts of waste is critical. "Big pharma companies prefer to use synthetic roots because they can scale rapidly. However, this involves the use of enormous amounts of organic solvents, which is environmentally deleterious," said Castor. "We prefer to work with plants and microorganisms because they provide ecological balance and sustainability."

For companies like Aphios Corporation, eschewing the norm attracts individual consumers who are interested in products that are designed in a way that mitigates impacts on the environment. To help companies with similar values develop their pipelines, TCG Lifesciences, a global CRAM, created its subsidiary company to serve as a contract innovation company that utilizes green and sustainable technologies. Aptly named TCG GreenChem, the CDMO offers an innovation center in the Virginia Biotechnology Research Park with access to a green technology innovation center with novel platforms for catalysis and continuous flow processes. "TCG GreenChem is positioned as a contract innovation company that provides CDMO services with a unique modus operandi in the space of supporting pharmaceutical R&D," explained Swapan Bhattacharya, managing director of TCG Lifesciences.

As environmental concerns grow amongst clients and their end customers, offering greener development and manufacturing processes is a smart way for CDMOs to stand out from their competitors. ■

**What has been driving growth for AMPAC Fine Chemicals (AFC) over the past few years?**
As the pharmaceutical sector continues to grow at a record pace, the growth of CDMOs that support these customers also grows. AFC is growing in all four of our locations – at our headquarters in Sacramento as well as our plants in Houston, TX, Petersburg, VA, and our AMPAC Analytical testing service site in El Dorado Hills, CA.

**Who are the typical clients that AFC serves?**
AFC primarily supports clients with projects in phase 2 clinical trials through to commercial manufacturing, as we are well known for our commercial launch capabilities and PAI readiness. That said, we certainly support earlier clinical phase candidates if they feature one of our core technologies, such as core processing, energetic chemistry, SMB chromatography, or high potency. With this in mind, we serve a wide range of companies from virtual pharma to large pharma and everywhere in between.

**Could you elaborate on the innovative technologies AFC leverages to provide its array of services?**
AFC is well known for its capabilities in energetic chemistry, and we continue to develop in this area. We invested in a safety laboratory to provide better data with the safety and manufacturing properties of clients' materials. Something that goes hand-in-hand with this is our flow capabilities and continuous processing capabilities, a space we have been operating in for several years. We continue to invest in our capabilities for continuous distillations, continuous isolations, or any other continuous reaction. We are also a leader in simulated moving bed (SMB) chromatography, which sees demands for purification of chiral materials.

As industry needs get more complex and specifications get tighter, analytical capabilities become more important. We have these capabilities at AMPAC Analytical and can support our customers as quality demands continue to increase.

> Outside of our manufacturing capabilities, AFC is investing and featuring AMPAC Analytical given the growing demand for pharmaceutical testing services.

# Jeff Butler

President
**AMPAC FINE CHEMICALS, AN SK PHARMTECO COMPANY**

**Where is the company investing in terms of its manufacturing capabilities?**
We continue to invest into our manufacturing facilities to keep up with the growing industry and the services our customers request. Over the past two years, we have seen tremendous interest in US-based manufacturing, with particular interest in our sites that produce critical medications as we have moved through the pandemic. We are also developing technologies in continuous processing and energetic chemistry.

AFC is investing into its multi-purpose expansion of equipment sets and continuous processing equipment that can complement the company's reaction bays and processing lines. We are bringing on additional reactor capacity, drying capabilities, solids handling capabilities, and continuous processing capabilities.

**How does being part of a larger global organization impact AFC?**
AFC is in a unique position, especially from our customers' perspective, in that we can support them from US soil. From this perspective, AFC is also in a unique position to supply the needs of the US government. That said, we are part of a larger parent company, SK pharmteco, which operates on a global scale. For this reason, we can also provide support to other governments.
Over the past two years, more attention has been placed on understanding supply chains and how geopolitical interests may have an impact. With SK Pharmteco as a global parent company, AFC has the unique ability to leverage relationships with our sister sites in South Korea and Europe to ensure we can continue to supply our customers. It is interesting to see governments and institutions realize the extent to which most basic raw materials, intermediates, and chemicals production is done in India and China. This will not change overnight. It will remain important to have dual supply chains to fulfill on promises to our clients.

**What will drive growth for AFC over the coming years?**
AFC continues to grow at all its sites to match increased demand in the company's assets and capabilities. We are also looking at featuring more prominently our analytics capabilities given the growing demands from our customers for testing services. We see a unique opportunity to expand these capabilities even outside of our manufacturing capabilities, which is why we continue to invest in AMPAC Analytical. ■





**Could you bring us up to speed on Cureline's operations?**
Our business operations became virtual during the pandemic, which resulted in accelerated company growth. With our effective small management team in California, we were able to expand our clinical network members abroad and conduct more projects in 2021. We expanded our operations in Ukraine and Serbia, increased our operational efficiency in Argentina, standardized operations in India, and continued working with our Chinese colleagues on projects related to the Chinese population. Overall, we spent the past two years developing closer connections to our clients, vendors, and clinical partners on a global scale.

Cureline always focused on people and technologies. In the past we have established and successfully grown Cureline BioPathology, a translational histopathology laboratory. Since 2019, Cureline Molecular Services, our San Diego-based company, offers cellular and molecular biology services that complement our HBS biorepository and histology laboratory in San Francisco.

Starting clinical operations in the EU in 2021 resulted in developing major research collaborations, developing unique metastatic tumor animal models and building a CRO working on advanced medical technology products (AMTP), including cell and gene therapy. Expanding into this fast-growing market aligns with our focus on making Cureline an outstanding Global Translational CRO.

**What types of customers does Cureline work with?**
Cureline's geographical expansion efforts deepened the company's client base, which historically includes over 700 accounts since 2003 and 50+ new client companies annually. In addition to pharma companies, we also work with US-based universities including UCSF, Harvard, Berkeley, and Stanford, as well as government institutions (NIH, FDA). In general, our clients choose to work with Cureline over bigger service providers due to our excellent understanding of science, collaborative project management, and attention to detail, especially with complex projects.

**How does the increased use of AI impact demand for Cureline's biospecimen products?**
The use of AI in data analysis will expand significantly to improve early detection across a variety of diseases, as it has in oncology. Unlike tech companies, however, the biomedical field has yet to fully capitalize on advances in AI and machine learning that can combine the specimens, conduct populational studies, and develop predictive models to understand the best and most economically viable approach. In the past year, we completed over twenty large projects for companies seeking to deploy the power of AI in this space.

> We spent the past two years developing closer connections to our clients, vendors, and clinical partners on a global scale.

# Olga Potapova

Founder, CEO & Scientific Director
**CURELINE**

**Could you describe how Cureline Molecular Services (CMS) facilitates precision medicine programs?**
CMS was established to facilitate genetic and biochemical characterization of biospecimens and provide drug screening and toxicology services using cell-based and 3D tissue-based assays for preclinical studies. Clients with limited access to technology use a broad spectrum of cell-based and molecular assays developed at CMS to outsource services and scientific projects. We help mid-size companies and virtual start-ups to process collected human biospecimens, isolate viable cells, nucleic acids and proteins, and to generate extensive data for development of their products internally. CMS is also a local service provider for firms specializing in animal studies. Such projects require localized assistance to help deal with complex logistics and the task of sending samples abroad.

Ultimately, the plan is to make CMS a laboratory that can provide consumer services where patients can obtain personalized medical data, including genetic and immune landscape profiling, and individual longevity products testing. The tests would help to predict therapeutic outcome and monitor response to treatment, drug effects, responses to antiviral drugs, or overall health. This ability to survey the overall landscape in metabolomics, proteomics, and immunomics could be the future of our molecular services. We aspire to work with clients who develop such products and members of the public who wish to learn more about their health.

**Beyond oncology, which therapeutic areas have you been tracking?**
Autoimmune diseases are the second biggest field after oncology, which is due to several reasons including the environment and stress. The inherited diseases field is also growing quickly with the intervention of new technologies like CRISPR gene editing. This informs our desire to build a CRO to work with AMTP clinical trials. Additionally, the pandemic has illuminated the growing prominence of infectious disease research and the imperative to develop vaccines effectively. Growth in different therapeutic areas will inevitably drive growth for Cureline as well, and we are excited about the prospect of increasing the number and variety of customers we are able to assist in bringing novel drugs and diagnostic tests to patients. ■

> We established a dynamic drug delivery systems (DDS) company focused on providing a range of effective solutions to optimize the delivery of pharmaceutical products.

# Satya Vadlamani

Chairperson & Managing Director
**MURLI KRISHNA PHARMA PVT LTD**

**Can you introduce yourself and your journey to making Murli Krishna Pharma (MKPPL) the company it is today?**
I am an electrical and electronics engineer, and I started my pharmaceuticals career as an export manager at Armour Chemicals in 1992. I later joined Biochem Synergy, and in 1996, started work for Ajanta Pharma in the capacity of general manager for international marketing. At the time, I was the youngest female general manager in a market predominantly dominated by men. In 1998, I established Murli Krishna Exports, a pharmaceutical API's marketing and trading company. Opportunities in the pharma market were increasing, which led me to start a new venture in manufacturing and semi-finished formulations, so Murli Krishna Pharma was born. The company was founded by Dr. Vijay Shastri and myself on 1 April 2004.

**What kind of manufacturing capacity does MKPPL possess?**
We have a world-class oral, solid-dosage manufacturing facility for pellets, micro-pellets, and granules, which was commissioned in 2005 and approved by the European Union (EU) and for GMP compliance by the WHO. Our plant has also been approved for compliance by major pharma companies such as Mylan, Sanofi, Dexcel, and Pfizer. Today, MKPPL has EU approval for 20 molecules, four potential IPRs, and a supply agreement with one of the leading generics companies. The company also has DMFs filed for most of our products in the US. Over the last few years, MKPPL has won a number of awards including the 'Made in India' award in 2016 for the fastest growing pharmaceutical company in the country. We want to continue our success and would like to be known as one of the leading global research-based, drug-delivery companies, with an expertise in novel drug delivery systems, constantly striving towards building and strengthening our intellectual property.

**Can you elaborate on MKPPL's product portfolio and which products and services are driving growth for the company?**
We currently have a focus on nanoparticle products. Our product portfolio includes alpha blockers, anti-depressants, anti-fungal products, inhibitors, digestants, anti-inflammatory products, anti-coagulants, anti-ulcerative products, immune suppressants, anti-obesity products, vitamin supplements, anti-cancer products, antibiotics, and lipid regulating agents.

We take pride in developing formulations with thoughtful selection of matrix and cogent selection of polymers. We select the matrix based on the physicochemical properties of the drug molecule and develop products using an aqueous base instead of organic solvents to avoid toxic effects that might arise from organic solvents.

**How has MKPPL's focus on nanoparticles evolved over the years?**
Our R&D division has innovative techniques to allow water-soluble drugs to be layered using aqueous media. MKPPL has developed safe nanoparticles that encapsulate micronutrients and interact with the outermost layer of skin to enhance penetration and can be delivered through an oil platform. Our liposomal nanoparticle approach can be utilized for administering vitamins through the dermal route and delivering antibiotics and anti–inflammatory agents through topical applications. We have developed a transdermal oil for treating patients suffering from malnutrition, especially kids suffering from anemia.

Nanoparticles can also be effectively used for the manufacturing of ointments, such as our tacrolimus product, and solutions, such as everolimus. MKPPL has also developed a nanoparticle-based matrix which can deliver hydrophilic as well as hydrophobic drugs, using a combination of hydrophilic and hydrophobic excipients as a clear solution. This use of excipients ensures that the drug is absorbed optimally, and the nano particles ensure that the drug penetrates not only through the hydrophobic and hydrophilic channels but also through the ora serrata, which protects the eye from any foreign body entering the optical cavity.

**What is MKPPL's vision for the future?**
We are a fast-growing company and hope to double our business within the next year. We have the objective to significantly advance our transdermal oil segment and plan to leverage our expertise in nano-solutions to implement technological innovations for the delivery of micronutrients using fortified oils. We believe that our transdermal oil products will be one of a kind in the market, and we want to offer a complete technical package for registrations in all regulated and semi regulated markets. We are open to forming strategic partnerships to assist us in clinical trials and help take our flagship product to market. The US is one of our most important markets as they understand and support R&D. ■





> The main trait we are looking for in partners is access to interesting chemical libraries where combining good chemistry with our platforms we can identify novel treatments for neuropsychiatric disorders.

# Emer Leahy

President & CEO
**PSYCHOGENICS**

**Can you give an overview of how business has evolved for PsychoGenics over the past year?**
There are two sides to PsychoGenics: a preclinical CNS-focused CRO and drug discovery. On the CRO side, PsychoGenics experienced significant growth with our service business growing about 30%. This can largely be attributed to the significant amount of investment currently going into CNS research. More companies are being formed, and we are increasingly seeing small, well-funded, venture-backed companies reaching out to us for our services. We have continued to expand the company's service offerings and added many people to our team (currently 150). We have also increased our research facility footprint. On the drug discovery side, PsychoGenics has pioneered the use of AI in phenotypic drug discovery with our SmartCube and other in vivo platforms. We are seeing renewed interest from companies looking to partner with us in order to access our phenotypic platforms. We have also put significant effort into internal drug discovery where we utilize our platforms in psychiatric drug discovery. We have built up a substantial library of chemically diverse compounds (more than 7,000) that have been tested in SmartCube and have shown interesting activity for CNS indications. We have initiated several drug discovery programs and expect to take one or two of these into IND-enabling studies in 2022.

**Do you believe the need for CNS research and drug discovery has been exacerbated due to the pandemic?**
We definitely saw an increase in the number of people suffering from depression, anxiety disorders, PTSD, and anorexia in teens, amongst others. This has been particularly evident in the vulnerable adolescent population which showed an approximate 30% increase in the prevalence of mental illness compared to prior years.

**How would you describe the investment climate in the life sciences sector, particularly for CNS research and development?**
In 2020 and 2021 we saw a significant increase in investor interest and funding in CNS research. Many new well-funded companies emerged. Many big pharma renewed their interest in CNS research over the past few years. The government is also investing in certain areas of CNS research such as the NIH HEAL Initiative addressing the opioid crisis. PsychoGenics is part of the HEAL initiative through the Preclinical Screening Platform for Pain (PSPP), a government program initiated in late 2019 to help identify non-opioid analgesic drugs. This program is open to companies and academic institutions worldwide who can apply to NIH to have their assets screened in the PSPP platform.

**Can you elaborate on PsychoGenics' partnerships and collaborations within the sector?**
We have partnered with many companies to help identify novel and safe treatments for psychiatric conditions. Our partnership with Sunovion has been particularly productive with four compounds advancing to clinical trials. Ulotaront, previously known as SEP-363856, is the most advanced and is in multiple phase three trials for schizophrenia. Ulotaront is a new mechanism of action, and results from phase 2 suggest it has effects on negative symptoms (apathy and social withdrawal) with placebo-like side effects. We have also partnered with Roche, Blue Oak, and Karuna Therapeutics to identify potential novel drug candidates for the treatment of severe neuropsychiatric disorders. The main trait we are looking for in partners is access to interesting chemical libraries where combining good chemistry with our platforms we can identify novel treatments for neuropsychiatric disorders.

**In terms of AI, how has PsychoGenics been able to navigate processing big data into actionable tasks?**
AI has become a buzzword in the industry, but it is important to ensure that you are working with an AI-based platform that has been validated. PsychoGenics started employing AI in biology in 2002 as a way to industrialize phenotypic drug discovery. We have since delivered many compounds to the clinic where, in the case of ulotaront, our preclinical findings were validated clinically.

**What is PsychoGenics' vision and objectives for the next few years?**
Our main objective is to advance several partnered and internal compounds to clinical trials so patients can ultimately get access to much-needed improved treatments. To do this we will continue to grow the company and bring in new capabilities. Although we are experiencing a very tight and extremely competitive labor market, we aim to expand our team with the best people to move our company forward. Currently we have 20 positions to fill. ■

Each service provider finds its own balance of diversifying, specializing and sophisticating its manufacturing capabilities to stand out in a sea of competition. From blow-fill-seal to biospecimens, below are companies that have invested into unique offerings.

"Cureline Molecular Services (CMS) was established to facilitate genetic and biochemical characterization of Biospecimens and provide drug screening and toxicology services using cell-based and 3D tissue-based assays for preclinical studies... We help mid-size companies and virtual start-ups to process collected human Biospecimens, isolate viable cells, nucleic acids and proteins, and to generate extensive data for development of their products internally."

**– Olga Potapova, Founder, CEO & Scientific Director, Cureline**

"Our R&D division has innovative techniques to allow water-soluble drugs to be layered using aqueous media. MKPPL has developed safe nanoparticles that encapsulate micronutrients and interact with the outermost layer of skin to enhance penetration and can be delivered through an oil platform. Our Liposomal nanoparticle approach can be utilized for administering vitamins through the dermal route and delivering antibiotics and anti-inflammatory agents through topical applications."

**– Satya Vadlamani, Chairperson & Managing Director, Murli Krishna Pharma Pvt Ltd**

"Our novel HSC Technology, an automated High-Throughput Self-Interaction Chromatography technology platform, cuts costs, time, and manpower needed to optimize formulations. We measure the second virial coefficient of the active pharmaceutical ingredient (API) in various excipients, and the data collected enters a neural network that scans for different combinations. The solubility process is reduced from one year down to just three months."

**– Larry DeLucas, President, Soluble Biotech**

"Our innovative liquid-liquid separators solve the most difficult separation problems with ease, eliminating the need to run batches at half capacity with slow settling times, allowing for continuous manufacturing. Our devices are directly scalable from lab to pilot to production, and customers like our products as they are easy to use and maintain with plug and play functionality at all scales."

**– Andrea Adamo, Founder & CEO, Zaiput Flow Technologies**

"Vetter manufactures orphan and ultra-orphan drugs in its active pipeline. Conversely, we see substances like insulin replacing GLP-1 analogue drugs for which we manufacture approximately 70 million syringes of the same kind. We have both small-scale and large-scale filling capabilities to serve customers in both the precision medicine and large-scale manufacturing spaces."

**– Peter Soelkner, Managing Director, Vetter Pharma International**

"Blow-fill-seal affords a higher level of sterility due to the containment and limited human interaction in the manufacturing process. This process also enables us to mold a container into unique delivery systems to achieve specific therapeutic solutions as well as attain a superior level of filling accuracy."

**– Paul Josephs, President & CEO, Woodstock Sterile Solutions**

"AFC is well known for its capabilities in energetic chemistry and we continue to develop in this area... Something that goes hand-in-hand with this is our flow capabilities and continuous processing capabilities, a space we have been operating in for several years. We continue to invest in our capabilities for continuous distillations, continuous isolations, or any other continuous reaction. We are also a leader in simulated moving bed (SMB) chromatography, which sees demands for purification of chiral materials."

**– Jeff Butler, President, AMPAC Fine Chemicals, an SK pharmteco Company**





**We pride ourselves in being a discovery engine that will hopefully build out a large portfolio of new chemical entities that can one day become marketed drugs.**

# Swapan Bhattacharya

Managing Director
**TCG LIFESCIENCES**

**How has TCG Lifesciences (TCG) evolved over the past year?**

TCG was founded in 2001 and has continually expanded its capabilities over the years. Today, we are primarily focusing on the discovery and development of small-molecule drugs. The biggest development over the last year has been the establishment of TCG GreenChem, our US subsidiary with operations in New Jersey and Virginia. We have also moved into the in-silico space and are taking it all the way to AI-driven drug discovery. TCG is also developing translational neuroscience research capabilities utilizing a novel human stem cell platform technology.

Our goal is to collaborate with industry and academia to continuously bring innovative therapeutics to the market. We pride ourselves in being a discovery engine that will hopefully build out a large portfolio of new chemical entities that can one day become marketed drugs.

**How important is the US for TCG?**

Currently, there is strong growth happening in the biotech industry, with a substantial amount of investment coming from venture capitalists focusing on different types of diseases. The FDA has been extremely swift in approving new chemical and molecular entities with an annual average of 51 new drugs approved in the past five years (compared to only 35 per annum in the prior five year period), and the trend continues in 2022. In addition, the US leads the world in drug innovation, largely due to the depth of biological knowledge and cutting-edge technologies emanating from academia. The federal government is promoting local manufacturing of APIs, and we are actively supporting these activities.

**How difficult has it been for TCG to attract and retain talent?**

Currently, TCG and its subsidiaries have approximately 1,100 scientists, of which over 280 have PhDs and the balance hold Masters degrees. The current global manpower shortage poses a great challenge as the drug development industry expands, and we felt the impact while setting up our facilities in the US. We are mitigating the challenge by relocating talent from our India team to the US, as well as sharing the work seamlessly across both locations. In India, we have established a strong ability to source talent from academia and impart robust on-the-job training, as well as hire trained scientists directly from the industry. The country has a good network and ecosystem of people which are focused on small molecule drug development.

**Can you elaborate on the newly established TCG GreenChem?**

TCG GreenChem, with Chris Senanayake, Ph.D. in the roles of CEO and CSO, was set up in the US to leverage the great R&D capabilities and expertise within the country. TCG GreenChem is positioned as a contract innovation company that provides CDMO services with a unique modus operandi in the space of supporting pharmaceutical R&D.

We established an Innovation Center in the Virginia Biotechnology Research Park with access to state-of-the-art facilities that offer a green technology innovation center with novel platforms for catalysis and continuous flow processes. We also focus on developing innovative processes for economical and sustainable manufacturing of APIs.

In New Jersey, we are located in the Princeton South Corporate Center where we have a state-of-the-art facility with unique process-research capabilities that include proper route design utilizing the "First Time Right" concept. We are leveraging the capabilities of the Automated Reaction Design and Flow Technology to accelerate drug development activities utilizing experimental design for reaction screening and engineering. We are involved in developing various catalytic technologies to aid route optimization, prepare intermediates, regulatory starting materials, and APIs. This Center also houses a cGMP kilo laboratory to rapidly scale up chemistry synthesis to support clinical trials.

**Can you elaborate on TCG GreenChem's work on Molnupiravir?**

Molnupiravir is a Merck drug that received EUA from US FDA recently. It looks promising as an orally bioavailable drug candidate for the treatment of Covid-19 as positive interim analysis of a phase 3 study demonstrated a reduced risk of hospitalization or death by approximately 50% compared to placebo for patients with mild or moderate Covid-19. TCG played a significant role in developing and scaling up a novel development scheme using a specific enzyme for regio-selective acylation followed by modification of the cytidine moiety and reduced the number of steps that helped decrease manufacturing costs. M4ALL, MIT, and TCG collaboratively established the sustainable and greener process for Molnupiravir for commercialization. ■

> CordenPharma's ultimate goal is to have sufficient capabilities and capacity for seamless support from early-stage through to commercial manufacturing.

# Michael Quirmbach

CEO & President
**CORDENPHARMA**

**In which ways has CordenPharma expanded its footprint over the past 18 months?**
CordenPharma is a full-service CDMO supplying APIs, excipients and drug products to the market. Over the past year CordenPharma has been extremely busy with supplying lipids to support vaccine manufacturing, as well as many other new products related and unrelated to Covid-19. We acquired three new facilities from Vifor Pharma related to oral solid dosage drug products and announced a large capex program where we invested heavily in new capacities and technologies, such as expanding our highly potent oral solid dosage drug product manufacturing at CordenPharma Plankstadt (DE). In addition, we signed a partnership agreement with Wacker to jointly develop know-how and manufacturing processes for formulating Lipid Nanoparticles (LNPs), and are in the process of building out our small-scale Peptide Centre of Excellence manufacturing unit in Frankfurt to support early-stage clinical trials with GMP manufacturing.

**How is CordenPharma involved with green chemistry?**
Green chemistry entails the methods we employ to reduce the use of certain organic solvents and how we run our processes more volume-efficiently than in the past. Because producing multiple hundreds of kilograms of peptides per year leads to an extensive amount of waste, the CordenPharma Peptide Centre of Excellence is collaborating with PeptiSystems, a Swedish-based developer of instruments for peptide and oligonucleotide therapeutic process development and manufacturing based on flow-through column technology. PeptiSystems has developed an innovative concept that allows for the manufacturing of peptides in a continuous mode, which reduces solvent consumption and corresponding waste by at least 40% in all peptides produced by Solid-Phase Peptide Synthesis (SPPS). The company has also invested in an expansion of our specialty lipids production using Supercritical Fluid Chromatography (SFC) technology for compound separation, an efficient and cost-effective process for purifying lipids and pharmaceutical drug substances. SFC is an eco-friendly and sustainable technique that utilises reclaimed CO2, coupled with online carbon dioxide recycling, resulting in a greener approach to manufacturing highly pure complex lipids.

**What impact will Astorg's recent acquisition of CordenPharma have on the company's operations or strategic direction?**
Currently our shareholders ICIG (International Chemical Investors Group) and Astorg are working to complete the transaction as quickly as possible and create a smooth transition for us. We do not anticipate any impact or changes to our current operations in the short term. Our recent conversations with Astorg indicate that they are fully committed towards the execution of the recently launched strategic CAPEX program at CordenPharma, as well as the long-term strategy of the Group as it relates to our five technology platforms.

**With a shortage of skilled labor across the board, how does CordenPharma attract and retain talent?**
The labor pool is often dependent on the country of operation and physical location of a company. In Colorado, despite significant competition, CordenPharma still managed to hire approximately 100 people in 2021. Quality talent is more difficult to attract in today's environment, and that is why we aim to be flexible and attractive to younger generations, offering good career opportunities and creating a company culture where people want to work.

**What is CordenPharma's vision and growth strategy moving forward?**
The US is the most important market for CordenPharma. Currently, we only have two sites in Boulder but would love to expand our manufacturing footprint within the country. Our business is structured around five Technology Platforms – Peptides, Lipids & Carbohydrates, Highly Potent & Oncology, Injectables, and Small Molecules – with the goal to provide fully-integrated services to our customers. The Vifor Pharma acquisition opportunity aligned well with our strategy to broaden our CDMO capabilities. For example, in our Small Molecule platform, we had only been heavily active on the API side but were lacking Drug Product capabilities. With the new acquisitions, we have closed the gap in our drug product offering with increased capabilities and capacities in the manufacturing of non-sterile speciality drug product dosage forms. With the addition of the three new facilities, the company's global network now consists of 12 facilities - 11 GMP sites and one R&D laboratory - supported by approximately 2,600 employees.

CordenPharma's ultimate goal is to have sufficient capabilities and capacity for seamless support from early-stage through to commercial manufacturing. Through our growing network of cGMP facilities across Europe and the US, we aim to continue to translate complex processes and projects at any stage of development into high-value products. ■





# Peter DeVoung

CEO
**PIRAMAL PHARMA SOLUTIONS**

**How was 2021 for Piramal Pharma Solutions?**
2021 was a great year. We grew our organization by several hundred employees across our global organization to help meet the strong demand for our products and services. Despite the challenges of the pandemic, we continue to increase our capacity and capabilities, particularly in the areas of drug substance including high potency APIs, peptides, gene therapy, vaccine development, and monoclonal antibodies.

Our development-oriented API services have been in very strong demand, as well as our Antibody-drug Conjugates (ADCs). Additionally, we are expanding our sterile fill-finish and peptides offerings.

**Can you provide an overview of Piramal's current capabilities in the US?**
Our Riverview, Michigan API facility provides development and commercial manufacturing support, including a differentiation on high potency. We are in the process of a significant expansion here that should be completed by early 2023. Our Lexington, Kentucky facility is for sterile fill and finish. We also recently added a facility in Sellersville, Pennsylvania, to further integrate our offerings and be able to offer drug product as well. We continue to keep our eye out for new acquisitions to complement our strong organic growth plans and track record. ■

# Paul Josephs

President & CEO
**WOODSTOCK STERILE SOLUTIONS**

**Could you introduce our readers to Woodstock Sterile Solutions?**
Woodstock is a CDMO that was carved out from the pharmaceutical company Catalent in April 2021. We specialize in blow-fill-seal technology (BFS), which is sterile manufacturing produced primarily in a unit dose plastic container.

**What are the core benefits of BFS technology and its main use cases?**
BFS affords a higher level of sterility due to the containment and limited human interaction in the manufacturing process. This process also enables us to mold a container into unique delivery systems to achieve specific therapeutic solutions as well as attain a superior level of filling accuracy.

We use BFS technology primarily for ophthalmic and respiratory cases. However, it can be used to administer oral liquids by extending the mold to deliver an oral medicine into the back of the user's oral cavity.

**What is your growth strategy for Woodstock over the coming years?**
While our core will remain BFS technology, our growth plan includes selectively adding technologies that encompasses small volume parenteral, prefilled syringes or multidose ophthalmic. Furthermore, we are investing US$5 million in a new quality control lab to service our customers,. This will complement the addition of new sterile technologies through M&A. ■

# Jeff Reingold

COO
**CONTRACT PHARMACAL CORP (CPC)**

**Can you give an overview of Contract Pharmacal Corp?**
Contract Pharmacal Corp (CPC) is driven by the mission of setting and raising the standards in contract manufacturing/packaging and pharmaceutical development. The onset of the pandemic brought along many challenges with some, such as supply chain and logistics disruptions and skilled labour shortages, continuing into the present day. We had to be creative and quickly adapt to navigate through the challenges and are working hard to not only retain the people we have, but also recruit and attract new talent to our company. We had to get much more involved in our vendor relationships, just as our customers had to get much more involved with us in terms of the entire process.

**Which industry trends will CPC be focusing on for the next few years?**
CPC's growth has been in the Rx, OTC and dietary supplements sector, and we see these sectors only continuing to grow. The pandemic opened people's eyes to the importance of dietary supplements like vitamin C, vitamin D, vitamin B12, and zinc. CPC's primary focus is solid- dose manufacturing. Over the past two years we have added substantially to our production capabilities for this segment. ■

# A Post-Pandemic World

## Stronger supply chains and louder calls for reshoring

In addition to creating a host of new challenges, the pandemic revealed certain weaknesses within the industry that had been lying dormant for years. Challenges such as weak supply chains and the increased offshore production of essential pharmaceutical materials were brought to light as Covid-19 threatened the stability of the preexisting order.

"The concept of globalization as an unfettered path which everyone is going to pursue has certainly been challenged over the past two years, first with the pandemic and now with increasing geopolitical turmoil. This changes the way companies regard just-in-time production and the origin of raw materials," acknowledged Will Lewis, chairman and CEO of Insmed. While there is consensus that the sector cannot return to its pre-pandemic model, questions remain over how, and how much, things can change.

**Stronger supply chains**

As part of a complex and global industry, pharmaceutical supply chains are a complicated dance in which one misstep – any delay or mistake – can mean patients do not receive potentially lifesaving therapeutics. The past two years have revealed just how vulnerable the ecosystem is to disruptions and how important it is for companies, service providers in particular, to strengthen their supply chains.

One obvious way to strengthen a supply chain is to shorten it. Companies like New Vision Pharmaceuticals did this to eliminate friction and deliver on requests faster than companies developing products overseas. "We had a client approach us to work on a rapid Covid-19 test, wanting to produce a single-use vial for at home testing. It was only six weeks between when we had our initial discussion to when we had produced the product for them. We quickly made many millions of vials to support the rapid ramp-up," said the company's CEO, Alan Petro. "If they had attempted to do this with an offshore supplier, it would have taken the same amount of time just to get the product across the ocean and through ports. This level of responsiveness has been our focus."

Other companies focused on improving channels of communication with customers and vendors to be able to react faster to challenges and establish contingency plans. For Jeff Reingold, COO of Contract Pharmacal Corp, information is key. "Understanding and keeping a pulse on the environment and what is happening is essential. One of the major benefits of CPC is that we have offices and boots on the ground in the US, China and India, which gives us the ability of real time information sharing of what is happening in the critical markets that service our business," he said.

In addition to being able to react more deftly to supply chain disruptions, getting ahead of challenges is a smart way to prevent problems down the line. For Ascendia Pharmaceuticals, asking for more up-front information from clients has enabled them to proactively source with greater accuracy. "Ascendia asked its clients for permission and openness to start getting ahead of the power curve specific to certain supplies that would be critical for their future needs," explained Robert Bloder, the company's chief business officer. "Our clients' effective communication gave us a window to strategically procure the necessary materials and components to get product to the clinic on time and get patients dosed."

Given the manner in which several service providers were able to restructure their supply chain organization in response to the pandemic, it appears that Covid-19 served as a catalyst for a shift that will remain long after the pandemic has subsided.

**Make America pharma again**

In addition to either shortening supply chains or creating strength through redundancy, some companies took the pandemic as an impetus to move operations altogether.

The desire to reshore manufacturing capacity has been a popular cry within the life sciences since before Covid-19 brought the theme to a boiling point. Over the past several years, increased outsourcing has gone to companies in countries like India and China that have strong manufacturing capacities and cheaper labor. While companies may enjoy the lower associated costs, the offshoring of pharmaceutical manufacturing has the potential to threaten the security of the nation's drug supply.

In 2019, the FDA issued a testimony before the House Committee on Energy and Commerce highlighting the importance of safeguarding pharmaceutical supply chains in a global economy. According to the administration, "The security of the nation's drug supply rests on three main factors: freedom from dependence on foreign sources of APIs, the resilience of our domestic manufacturing base, and the reliability of the facilities that make products for the US market."

Early in the pandemic, renewed concerns arose about the relative independence of the US' pharmaceutical supply when overseas manufacturers halted their supply to the country in order to focus on their own domestic needs. India, historically a reliable partner, has raised eyebrows on a few occasions. In early 2020, the country temporarily placed an export ban on several critical medications, and in 2021, it redirected its Serum Institute of India to reprioritize the production of the AstraZeneca vaccine for its own domestic needs. More broadly, transportation-related problems such as limited capacity and congestion in US ports have had consequences for product timelines and financials.

While this tendency towards offshore manufacturing had been going on for several years, it reached some people's attention for the first time as a result of Covid-related turmoil. "It is interesting to see governments and institutions realize the extent to which most basic raw materials, intermediates, and chemicals production is done in India and China," commented Jeff Butler, president of AMPAC Fine Chemicals, an SK pharmteco Company. "This will not change overnight."

As customers of service providers increasingly call for greater reshoring efforts to circumnavigate these challenges, some CDMOs have benefited. According to Tom Sellig, CEO of Adare Pharma Solutions, his company saw a spike in demand for its services. "This trend, which is largely triggered by the rising cost of transportation and inflation, has benefitted Adare. The company recently had six clients in one week alone reach out to move a large portion of their US production onshore," said Sellig.

Of course, moving operations from a manufacturer in one country to another is easier said than done. "The key stakeholders in each country we operate in are pushing for increased local production," said Peter DeYoung, CEO of globally operating Piramal Pharma Solutions. "The challenge now is how this will be funded. Every major government has put tremendous stimulus into their economies during the pandemic and now they must grapple between the desire to have domestic production and figuring out where to spend limited resources."

DeYoung has witnessed this tension play out in different arenas. He noted that companies serving US patients are seeing strong demand for development and production for specific therapy areas, particularly those targeting

## Peter Soelkner

Managing Director
VETTER PHARMA INTERNATIONAL

**Can you introduce Vetter and highlight the company's key achievements over the past year?**
Vetter is an established family-owned CDMO in the fill and finish space with a focus on aseptic filling and packaging of a variety of containers including syringes, vials, cartridges, and dual-chamber applications. Over the last few years, we have also focused on our Vetter Development Services (VDS), where we entertain approximately 250 projects in clinical stage at our sites in Skokie, Illinois, and our new site in Rankweil, Austria. Vetter has a global team of 5,700 employees from more than 60 different nations, of which approximately two thirds are women. In 2021, we put additional cleanrooms into operation, broke ground for more expansions at our sites, and implemented more automated visual inspection machines in our center of visual inspection and logistics.

**How does Vetter navigate shifting demand towards targeted development required for precision medicine and more large-scale requests?**
Looking at projects which have received FDA approval, there is an array of orphan drugs and ultra-orphan drugs which highlight a trend towards creating molecules for targeted populations of only a few thousand patients worldwide. Vetter also manufactures orphan and ultra-orphan drugs in its active pipeline. Conversely, we see substances like insulin replacing GLP-1 analogue drugs for which we manufacture approximately 70 million syringes of the same kind. We have both small-scale and large-scale filling capabilities to serve customers in both the precision medicine and large-scale manufacturing.

**What are Vetter's goals for 2022 and beyond?**
We will strive for impeccable quality in delivering products that adhere to all regulatory requirements. Our mission will remain to provide reliable, efficient, and safe processes from development, aseptic filling, and visual inspection to parenteral packaging in an economically, ethically, and ecologically responsible manner. 2021 marked the first year where we were globally CO2-neutral based on initiatives such as the exclusive use of electricity from verifiably renewable energy sources, and we will continue to invest in sustainability initiatives. ■

## Jay Shukla

President and CEO
NIVAGEN PHARMACEUTICALS, INC.

**How has Nivagen navigated supply chain challenges that emerged as a result of the pandemic?**
We continue to see an increase in freight costs, delays in shipping, and added challenges to logistics in general. We started keeping at least four to six months of additional inventory in our warehouse. We are now also carrying more API inventory to generate the product, though many buyers in the US are still not willing to accept the resulting price increases. This has forced us to either work at lower margins or sometimes to even discontinue certain products – this is what we call gross margin pressure due to increased cost.

Another challenge we faced was that the FDA was not inspecting any facilities, so we have approvals that are on hold. We hope that in 2022 both logistics and FDA challenges will improve.

**In which ways has the generics landscape evolved over the past couple of years?**
There is a consolidation of wholesalers on the buying side while there are thousands of manufacturers on the selling side. This imbalance causes manufacturers to work at much lower margins than wholesalers, retailers, and intermediaries. Thankfully Nivagen mostly carries mature products that have already bottomed out, and we were able to raise funds in 2020. This liquidity allowed us to continue doing our R&D work and expand our pipeline. We are building a robust team that can collaborate creatively to generate new products.

**Is Nivagen planning for continued growth in 2022?**
We are currently in the process of completing our 100,000 sq ft, state-of-the art manufacturing unit here in California. We are also focusing on our 505(b)(2) programs, where we are exploring improving or extending the lifecycles of existing therapies. We are also working on vertically integrating all our products – all the way from APIs to commerce. Our plan is to continue to manufacture our own products and work as a CMO for other companies having supply chain difficulties. ■





smaller patient populations that often have higher price tags associated. On the other hand, drugs produced for larger patient populations are still being manufactured in Asia.

The issue of funding increased domestic production has led to complications for some companies. Nivagen Pharmaceuticals, Inc. is a generics company that shifted operations to confront supply chain issues resulting from Covid-19. "We started keeping at least four to six months of additional inventory in our warehouse. We are now also carrying more API inventory to generate the product, though many buyers in the US are still not willing to accept the resulting price increases. This has forced us to either work at lower margins or sometimes to even discontinue certain products," explained president and CEO Jay Shukla.

One of the main challenges of reshoring manufacturing is the need for domestic facilities to support such a shift. Rather than moving everything onto US soil, it is often just the final stages that make a return. In an eight-step synthesis, perhaps only the final two steps are moving back to the US. The fact remains that most companies in the US and Europe do not have capacities to do the first six in-country. As we begin to enter a post-pandemic world, questions remain over the extent to which operations will return to US soil. As the FDA goes back to live inspections instead of virtual, new considerations will enter the fold; companies may increasingly contemplate why they should set up facilities in the US where the FDA will almost certainly spend weeks conducting inspections when they could instead operate out of China or India, where the FDA would likely provide advanced notice before inspection and remain onsite for no longer than a week.

Despite these complications, the root concern – the security of the nation's drug supply – will not go away. With the rise of new considerations, such as geopolitical turmoil in Ukraine, safeguarding domestic supply of essential materials against foreign disturbances becomes all the more pressing. ■

**What were the highlights of 2021 for New Vision Pharmaceuticals (New Vision), and what have the impacts of the pandemic been on the company's operations?**

New Vision Pharmaceuticals was fortunate to have experienced significant growth in 2021. We have been developing relationships with mid-tier and large organizations for both tech transfer developments and fill-finish operations. We are also supporting significant OTC production for private label and branded products.

Given the supply chain issues that arose from Covid, there has been a strong push to shorten supply chains. New Vision has been particularly responsive to our clients' needs in this regard and we have been able to significantly shorten our supply chains, especially compared to products produced overseas. For example, we had a client approach us to work on a rapid Covid test, wanting to produce a single-use vial for at-home testing. It was only six weeks between when we had our initial discussion to when we had produced the product for them. We quickly made many millions of vials to support the rapid ramp-up. If they had attempted to do this with an offshore supplier, it would have taken the same amount of time just to get the product across the ocean and through ports. This level of responsiveness has been our focus.

**Can you elaborate on this desire from clients to reshore their manufacturing capabilities?**

We have observed an enormous effort to reshore manufacturing capacity, particularly as a result of limited transport capacity coupled with the congestion in US ports, which has consequences not only from a timeline perspective but also for bottom line financials. The cost to transport a container has increased four-fold, making it a serious factor to consider. Additionally, geopolitical turmoil such as the crisis unfolding in Ukraine is pushing many organizations to question the value of a far-flung global supply network.

**What are some of the benefits you see in blow-fill-seal (BFS) as a manufacturing process?**

> We had a client approach us to work on a rapid Covid test, wanting to produce a single-use vial for at-home testing. It was only six weeks between when we had our initial discussion to when we had produced the product for them.

# Alan Petro

CEO
**NEW VISION PHARMACEUTICALS**

The idea behind single-use vials is that the patient consumes all the contents. Often, people have medicine cabinets filled with expired products. With single-use vials, on the other hand, you purchase in smaller quantities and consume fully. BFS also makes products incredibly difficult to counterfeit, which is a serious issue on a global scale. This way, the purchaser has assurance that what they think they are purchasing is what they actually get.

**What trends have you observed in the adoption of BFS in the US?**

Some of the early adopters of BFS technology in the US have been hospitals, nursing homes and other large care facilities. From a medication control standpoint, these products are easier to measure and leave no waste left in the bottle. Additionally, we are seeing strong demand from the pediatric market. It is easier for a mother to carry various single-use, non-breakable vials rather than lugging around several bottles.

Additionally, the need for at-home Covid tests is increasing significantly, which seems to be an outcome of the lockdown period. People need medical care irrespective of the challenges they face in physically going to a hospital or clinician. Being able to receive a test through the mail that you can do at home represents the future of medicine in broader terms as well. A major shortcoming of the American medical delivery system is that while there is an availability of physicians in major metropolitan areas, there is a severe lack in more remote locations. We see a significant opportunity for telemedicine and at-home testing services to support the needs of these populations. In this way, blow-fill-seal has the ability to meet needs that were exacerbated over the past two years but have been systematically underserved within the American healthcare system for much longer.

**How will New Vision grow over the next few years to continue to meet the demands of its clients?**

New Vision will continue to focus on sterile and nonsterile pharmaceuticals, with our primary markets being ophthalmic, respiratory, and dermatological. We are also seeking partnerships to utilize our large open clean room capacity. Additionally, the company will increase its product development teams to be able to work with a number of different clients that may have great ideas but not know how to bring them to the marketplace. This is where New Vision truly has the potential to make an impact. ■





**How was 2021 for Quotient Sciences, particularly within the US?**

In February 2021, Quotient Sciences expanded its portfolio of services to include drug substance and bioanalysis capabilities by acquiring the AInwick facility from Arcinova, a UK-based CDMO. Over the past year we have been focused on fully integrating these capabilities into our core Translational Pharmaceutics platform, saving our customers significant time and costs by integrating drug development and clinical testing services within a development program under a single clinical protocol. We also went through a series of organic investments at five of our seven sites, where we have been increasing drug substance, clinical trial manufacturing, and clinical testing space. These investments have either been completed or are ongoing and will be completed in 2022.

In recent years, there has been phenomenal investment in pharmaceutical R&D, and the number of molecules continues to grow. Aligned with this increase, Quotient Sciences' customer base has grown to approximately 500 customers across the US and Europe. We have operating sites in both the UK and the US, but 80% of our revenues are generated from US-based customers.

**Can you explain the importance for drug developers to have a CDMO that can manage both drug substance and drug product in parallel?**

Quotient Sciences wants to support our customers with their molecules earlier in the development process, from the point at which the drug candidate molecule is selected from the discovery program. By incorporating our scientific expertise and development technologies at an early stage we can help them make the most data-informed decision possible. We can then implement a seamless program of work that integrates drug substance synthesis and manufacturing into our Translational Pharmaceutics platform to provide time and cost savings.

**Have you noticed increased interest in the development of more targeted drugs?**

Approximately 50% of drugs approved by the FDA over the past five years have been for orphan/rare disease indications. This presents a unique challenge and opportunity to the industry, as historically service providers and pharmaceutical companies looked for big blockbuster drugs that would be prescribed to millions of patients. Today, patient populations are becoming more targeted with an increased focus on rare diseases. To support this, supply chains must be more flexible. When we manufacture a product, the customer then delivers it to patients, either in clinical trials or on the market. In the case of products for orphan diseases, the customer can either make a significant upfront investment and manufacture a large amount of product with an extended shelf life, or wait until patients have been recruited and deliver the product on an almost just-in-time basis. Quotient Sciences has created the protocols and methodology to just-in-time manufacture, package, label, ship and deliver product to clinics within a two-week time frame. With this model, managing the supply chain and logistics is fundamental. We are currently looking at acquisition targets that will help us bridge more firmly into this space, given our belief that just-in-time manufacturing will play an integral part in the future of drug manufacturing, specifically in more specialized and targeted therapeutic areas.

**At what stage of the drug development process is the element of speed or integration most critical to customers?**

Our principal focus is on the early phases of drug development, from the point of candidate selection through to proof of concept. Through the eyes of a drug developer, this phase of development is loaded with risk. This process is more difficult if the customer is working with multiple outsourced parties. The focus of our integrated Translational Pharmaceutics programs is to provide the customer with a development platform capable of responding in real-time to emerging development data and maintain an overall timeline to proof of concept.

**Quotient Sciences is investing US$8 million into expansion efforts for in-house API synthesis and manufacturing. What is the company's goal with this investment?**

We have seen increased demand towards local API production in both the US and the UK due to supply chain challenges caused by the pandemic and geopolitical issues. Our API capacity expansion will allow us to manage the drug substance and drug product supply chains in-house for our customers and ensure that APIs are supplied on time and at the right quantity and quality to drive the development program. ■

> Quotient Sciences wants to support our customers with their molecules earlier in the development process, from the point at which the drug candidate molecule is selected from the discovery program.

# Mark Egerton

CEO
**QUOTIENT SCIENCES**

We were excited to secure equity investment from Signet Healthcare Partners and have since almost doubled in size in both our capacity and talent pool.

# Robert Bloder

Chief Business Officer
**ASCENDIA PHARMACEUTICALS**

**Can you provide an update on Ascendia Pharmaceuticals' activities over the past year?**
2021 was an extremely busy year for Ascendia. We were excited to secure equity investment from Signet Healthcare Partners and have since almost doubled in size in both our capacity and talent pool. We were looking for the right opportunities to take the leap to expand our capabilities, and the partnership with Signet gave us the funds to mitigate significant supply chain disruptions, enabling us to place our orders for equipment and follow through with our delivery promises. We expanded our facility from 27,000 to 60,000 square feet and continue to increase our sterile and non-sterile GMP capabilities.

2021 was record-breaking in terms of revenue, bookings and billings. We continued operations through the pandemic and were fortunate to not shut down for a single day. As such, we could continue to provide important oncological, cardiovascular and CNS-related services, and we are working on expanding our capabilities into commercial within the next year.

**What innovative trends in the life sciences is Ascendia currently focused on?**
Our technologies are designed for the vaccine space to help reduce injection site reactions, an important aspect when inoculating large populations as reactions can deter people from participating or following up.

Ascendia also encapsulates proteins, peptides, and biologics, allowing for protection from hostile environments in the gut or other areas. We are focused on what our technology can do for product profiles to be more accessible to the entire population, including the elderly and children.

**What does the drug clopidogrel demonstrate about the power of nano-emulsion technology?**
Clopidogrel is the "gold standard" for the treatment of acute coronary syndrome and is only commercially available as a solid, oral product, so administering it in an emergency situation when a patient is choking or with a compromised airway adds to the patient's issues that need to be resolved. Additionally, when delivered orally, there is a two to five hour delay in the time required for the medicine to become effective. Through our EMULSOL nano-emulsion technology, Ascendia has formulated the free-base form of clopidogrel into a stable nano-emulsion that has an onset of action in minutes in an injectable delivery.

**Can you elaborate on the benefits that Ascendia's AMORSOL and NANOSOL technologies bring to your clients?**
Our AMORSOL technology is used to produce amorphous solid dispersions, greatly improving a drug's solubility and dissolution kinetics. This technology yields pharmaceutical products with enhanced bioavailability, reduced food-effect, faster onset of action, and controlled release of poorly soluble drugs. With NANOSOL, our nano solutions technology, we can control stability in solutions and droplets for a longer period and significantly increase the surface area available for dissolution. These nano-solutions can be so small that they appear as clear as water, making them more desirable in ophthalmic applications. We are very interested in leveraging this technology in the ocular space.

**How would you rate New Jersey as a regional hub for innovation in life sciences?**
The life science industry is immensely impactful for the state of New Jersey and extremely influential on its people, particularly the work done by organizations such as BioNJ. While innovation is global and the pandemic has shown us how much can be accomplished in a virtual environment, geographical footing is still critical. In New Jersey there is a wealth of institutional knowledge matched with state-of-the-art resources, allowing for truly impressive innovation where organizations like BioNJ are making great progress in connecting patients and families to ground-breaking accomplishments that can improve the quality of life for many of us who call New Jersey home.

**Looking into the future, how will Ascendia grow its operations?**
Ascendia will work on maintaining its strong company culture signified by BEST (Brilliant technology, Excellent service, Superior quality, and Trust) while simultaneously scaling its technological capabilities and workforce to meet client needs. Customers who come to us with a problem and leave with a solution often return because of the trust we have built. We aim to grow with our customers, becoming an integral part of their strategic plans by greatly enhancing their product portfolios and pipelines. In terms of our offerings, we will continue to expand our sterile technology for vaccines, proteins, peptides, and biologics. ■





# Patricio Massera

CEO
**AGC BIOLOGICS**

**What does AGC Biologics' footprint in the US look like, and does the company plan to expand here?**
The company's headquarters is in Seattle, where we have added new buildings for mammalian, microbial, and Covid-related projects. We recently acquired two sites in Colorado – one in Boulder and one in Longmont. The Longmont site, which we acquired to expand our cell and gene therapy services, is extremely large. This acquisition came after a deal AGC Biologics did in Milan in 2020 where we acquired MolMed, a company with a strong bioreactor and cell therapy platform, which we are now leveraging in our Colorado facilities.

Colorado is an amazing area to be located as the quality of life is high, there is an excellent biotech ecosystem, and great support from the government and life science organizations.

**Can you speak to the target profiles of the types of companies AGC Biologics works with?**
Today, we have 96 customers in our network ranging from very small virtual pharma companies to large, global pharma organizations. We offer world-class drug substance development and manufacturing services for mammalian and microbial based therapeutics, as well as multiple cGMP manufacturing lines at a variety of scales according to customer needs. We are also growing our capabilities in the cell and gene therapy space.

**How has AGC Biologics supported initiatives that mitigate the spread of Covid-19?**
We currently have eight projects related to Covid-19, dealing with prevention in terms of manufacturing vaccines or supplying vaccine components to customers. For example, we supply plasmid DNA materials to BioNTech for the Pfizer-BioNTech vaccine. We also have a contract with Novavax to manufacture Matrix-M, the adjuvant component for their Covid-19 vaccine.

**What types of technology is the company currently investing in?**
We are developing a new generation monoclonal delivery platform that can eliminate all non-disposable or single use steps. We are also working in cell line development, trying to improve the titers and the capabilities of the cell lines we offer. ■

# Timothy J. Miller

CEO, President & Co-founder
**FORGE BIOLOGICS**

**Can you give an overview of Forge Biologics and the company's main activities in the past 12 months?**
At Forge Biologics, we aim to help our clients move faster to clinical trial through implementing innovative technologies such as large scale bioreactors and automation. We are a gene therapy-focused CDMO and our mission is to enable access to life-changing gene therapies, taking them from idea into reality. A notable milestone for the company in the past year was raising an additional US$120 million in a Series B funding round, which enabled us to accelerate our expansion strategy to meet growing demands. We are expanding our existing AAV manufacturing capabilities and by Q3 2022, we will have 20 cGMP rooms available for manufacturing that can utilize 50, 500, 1,000, and 5,000 L bioreactors. The two 5,000 L bioreactors are some of the largest in the industry and are a huge value-add for large-scale client needs in clinical and commercial programs for use with Forge Biologic's proprietary HEK 293 suspension Ignition Cell line.

In January 2022, Forge Biologics secured another US$80 million non-dilutive credit facility with MidCap Financial which will further support our planned expansion of cGMP capacity, new client offerings, and platform development.

**Can you elaborate on the company's pipeline for FBX-101?**
We are currently in the process of screening patients for our Phase 1/2 RESKUE trial for patients with Krabbe disease. FBX-101 utilizes AAV gene therapy after hematopoietic stem cell transplant (HSCT) to deliver a functioning copy of the GALC gene, which encodes an enzyme needed to prevent the build-up of psychosine in myelinated cells of both the central and peripheral nervous system. This AAV therapy is a first of its kind in the world following the use of transplant, which is the standard of care, and intravenous AAV gene therapy infusion has the potential to overcome some of the immunological safety challenges of traditional AAV gene therapies. ■


# Chemicals Producers and Distributors

## Chemicals providers play a crucial role equipping their customers with the appropriate materials and processes to meet a changing landscape

Image courtesy of Brenntag.

Just as CDMOs are diversifying their capabilities to meet their clients' ever-complexifying demands, providers of chemicals solutions are working to stay ahead of new market trends based on the desires of pharma companies and their end customers.

As drug molecules both small and large become more difficult to formulate, formulators require new tools to work with. BASF Pharma Solutions works on producing novel excipients like its Kollicoat Smartseal 100 P for efficient taste masking and its Soluplus, the first polymeric solubilizer and matrix forming polymer. This type of innovation is not without its challenges, however. As David Freidinger, vice president of global business management for BASF Pharma Solutions pointed out: "Producing innovative and novel excipients remains challenging and comes with significant business risk. Regulatory agencies historically look at excipients as the sum of the formulation rather than individually, complicating the process. Our hope is that a dedicated excipient registration and qualification process helps overcome risk adversity and enables more innovative investments in the space."

In addition to stringent regulatory concerns inherent to the therapeutics ecosystem, shifting consumer demands are top-of-mind for business leaders of chemicals companies. Roquette has long offered plant-based ingredients made as by-products from the starch extracted from corn, wheat, potatoes and peas. As one of the largest excipients suppliers in the world, Roquette is the largest producer of ingredients that go into meltables, tablets that melt in the patient's mouth, according to Paul Smaltz, VP global business unit pharmaceuticals. Smaltz noted that it is his company's nutraceutical offerings that have been receiving particular attention recently.

Over the past few years, consumers have taken an increased interest to nutraceuticals as people begin to pay more attention to their overall health. "Increasingly, people want to make choices at the pharmacy that impact what they put in their bodies, such as deciding between a plant-based soft gel or an animal derived product," said Smaltz. "With the pandemic, people are more conscious than ever about what they put in their bodies and how to stay healthy."

Ultimately, however, chemicals providers and their customers are not concerned simply with what goes into these molecules, but also how they are made. ESG is more crucial than ever, and Lars Schneider, president of Brenntag Specialties Americas, who received an award from the non-profit Water for People in 2021 in addition to being appointed to its leadership council, provides a good example. "Some of the projects at Brenntag include optimizing the supply chain of customers and suppliers with the impact of CO2 reduction or building a supplier base that in its majority maintains a sustainability program, as well as introducing green energy and circular economy into our processes. For example, we have committed ourselves to 100 % green electricity by 2025," explained Schneider.

Chemicals providers play a crucial role in the value chain, equipping their customers with the appropriate materials and processes to meet a changing landscape. ■

> Roquette is currently seeing demand rise again for its pharmaceutical offerings as economies are opening up. For example, from the second half of 2020 through 2021, demand for cold and flu medications was 2% of what it historically is. Now that families are interacting again, demand is coming back.
>
> **– Paul Smaltz, VP Global Business Unit Pharmaceuticals, Roquette**

**Project Brenntag and our supply chain capabilities have certainly supported us, providing a clear focus between our different businesses and specializations to grow in the pharma and life science markets.**

# Lars Schneider

President of Brenntag Specialties, Americas
**BRENNTAG NORTH AMERICA, INC**

**What are the main initiatives that Brenntag has been involved in within the US pharma space over the past year?**
We have invested in our technical teams and resources to better understand our customers' needs. This also included operational investments into value-added services such as Pharma and Life Science conform custom packaging and blending, as well as the expansion of our product portfolio for the industry.

More broadly, we launched our internal transformation process we call "Project Brenntag" about a year ago to further enhance our value offering to our customers and suppliers. With this, we formed two business units: Essentials and Specialties. Within our Specialties business unit we have formed various focus industries, which allowed us to fully leverage our technical capabilities and provide a deep and specialized offering to our customers. We have also invested strongly in our supply chain by augmenting our technological and logistical capacities to further develop our strong logistic network and forecasting and replenishment capabilities.

**Which products do you see as key drivers of the company's growth within the pharma sector?**
We see a solid demand across the board, which starts from the process chemical side, solvents, but more specifically raw ingredients, excipients, actives, and the attending services. For us it is important to be able to provide the ingredients to an entire formulation under strict and consistent quality and regulatory assurances. This also holds true for any value-added services, such as packaging and blending.

**Brenntag reported a 19.6% increase in its operating gross profit in 2021. What factors were responsible for this growth, and how do you view the US market evolving?**
Project Brenntag and our supply chain capabilities have certainly supported us, providing a clear focus between our different businesses and specializations to grow in the pharma and life science markets.

Beside the product and service offering in combination with reducing complexity on the customer's side, we are able to tailor and guarantee a global consistent quality assurance, which is clearly critical in the pharma space due to our global footprint and set-up.

**Last year, you received an award from Water for People and appointment to the non-profit's leadership council. How has your commitment to sustainability impacted the company's operations?**
We have developed a brand new ESG strategy that considers our whole value chain from our suppliers, our own operations, and also the products that we offer our customers. It entails not only reducing the $CO_2$ emissions, but also other aspects such as supporting diversity, equity and inclusion of more sustainable products like biobased or recycled materials. Recently Dr. Andreas Kicherer has joined our global management team as Vice President Sustainability for Brenntag Group.

Some of the projects include optimizing the supply chain of customers and suppliers with the impact of $CO_2$ reduction or building a supplier base that in its majority maintains a sustainability program, as well as introducing green energy and circular economy into our processes. For example, we have committed ourselves to 100 % green electricity by 2025.

We do not rely on our self-assessment in this important field of ensuring a future for us and the ones to come but have been the first chemical distributor to join the UN Global Compact; we are member of the "Together for Sustainability" program and are being audited by Ecovadis on an annual basis, where we continue to hold gold status and achieve above industry ratings across various external sustainability review programs.

This allows for us to contribute to our society and community and hence, as management and employees, we are proud to be part of organizations such as "Water for People" anf various foodbank projects, among many others.

**What are most important US pharma initiatives for Brenntag for 2022?**
We aim to constantly grow our team of technical experts and our pharma dedicated service capabilities, ensuring quality compliance and consistency on the documentary side, as well as our USP and Good Manufacturing Practices (GMP) compliant services. Finally, we intend to remain well-informed of industry trends, from emerging dosage forms in the biopharma space to advances in the supplement subsector, in order to support our customers with formulation and registration. ■





**Drug molecules, both small and large, continue to become more difficult to formulate. To address these challenges, formulators need new excipients, and BASF has historically been one of the most innovative excipient suppliers in the marketplace.**

# David Freidinger

Vice President – Global Business Management
**BASF PHARMA SOLUTIONS**

**What was the highlight of 2021 for BASF's pharma business?**
Over the past three years, we invested significantly into upgrades of our equipment and processes, particularly at our world-class ibuprofen plant in Texas. Despite lower demand for ibuprofen due to Covid-19, the company is well positioned to meet customer demands as we shift to a post-pandemic world.

**How important is the US pharma segment to the company's overall operations?**
Pharma is a key strategic business unit for BASF, and pharma solutions represents one of the fastest growing market segments with some of the strictest quality and regulatory standards. While traditional pharmaceuticals like oral solid dosage forms continue to grow at a few points above the chemical industry, rapidly emerging market segments like biologics and cell and gene therapy are showcasing double-digit year-over-year growth rates.

The largest growth for the company's pharma segment will continue to come from the US, where the pharma industry is the global leader in innovation, research, and development of new drugs. BASF has significant commercial and technical pharma capabilities in the US that provide local collaboration and support, and we continue to invest in our US production sites to secure reliable supply in our range of APIs, excipients, and other ingredients.

**How is the excipient formulation space evolving?**
Drug molecules, both small and large, continue to become more difficult to formulate. To address these challenges, formulators need new excipients, and BASF has historically been one of the most innovative excipient suppliers in the marketplace. That said, producing innovative and novel excipients remains challenging and comes with significant business risk. Regulatory agencies historically look at excipients as the sum of the formulation rather than individually, complicating the process. Our hope is that a dedicated excipient registration and qualification process helps overcome risk adversity and enables more innovative investments in the space.

**Can you explain the benefits that BASF's Virtual Pharma Assistants bring to your clients?**
We launched our Virtual Pharma Assistants (VPAs) shortly before the pandemic as a digitalization suite of many of the best-in-class services we have historically provided for our customers. ZoomLab saves time during formulation, potentially reducing the number of resources required during the formulation development stage. What is traditionally a time-consuming and costly process is transformed into a digital experience where users input their active ingredients, dosage amount and dosage form to arrive at a first formulation within seconds. Customers can then move onto MyProductWorld to gather more information about the product, order samples and browse through assorted commercial functionality. This service is aimed at procurement managers. Integrated with both is RegXcellence, a comprehensive library of quality and regulatory documents and services that can provide users with global and country-specific compliance support, filing assistance, and the ability to receive alerts when documents are updated. We have seen clients end-to-end formulate a product, organize to select it, and get registration data, all achieved through the use of this robust platform. The concept of end-to-end self-service demand is being created through these digital tools, and the sales generated by these VPA services has been significant over the past two years.

All our VPAs now operate in over 90 countries, and their rollout has been a success story for BASF. They have led to an assortment of partnerships, many of which will be announced publicly throughout 2022.

**What will drive growth for BASF Pharma Solutions?**
We consider end-consumer preferences and behaviors to determine where to drive innovation. Within the excipient space, for example, we design products that help our customers to develop medicines that are more patient-centric, efficient, or easier to administer.

We will continue to expand our footprint in the biopharma industry with portfolio expansions and investments that will increase our capacity and unique capabilities in the market.

Additionally, we will continue to regularly release new modules for our VPA platform. We are also digitalizing our core manufacturing sites and launching virtual auditing experiences at our flagship ibuprofen plant in Texas, offering customers the opportunity to audit the facility even if they are unable to go in person. ■

# TECHNOLOGY SERVICES

"The pharmaceutical sector is historically slow in adapting to change, particularly digitalization. The pandemic forced this transition. There is now a recognition of how powerful it is to understand the nuances of data."

**– Jo Halliday,**
**Founder & CEO,**
**Talking Medicines**

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Image courtesy of Quotient Sciences

# Life Sciences Go Digital

## Turning to the cloud


Image courtesy of Talking Medicines.

Despite their cutting-edge prowess in many other regards, pharma companies in large part lagged behind other industry peers in the adoption of cloud technology and other emerging tools mainly due to concerns over data privacy.

"Most life sciences companies now agree that cloud-based technologies add value," asserted Infionic's CEO, Subramanyam SP. "There remains apprehension about using shared cloud databases, so a mid-way solution is a private cloud."

Infonic has made many implementations in pharma on the cloud that follow a model similar to a private cloud format, meaning the application and database are connected to only one company. In this way, Infionic offers its ERP solution as well as its electronic document management system to cover the document's lifecycle.

The heightened acceptance of more digital platforms has boosted demand for companies like RxS that offer prescription drug sampling services and technology, including tools for rep sample management, healthcare dedicated contact center services, and digital, client, and patient engagement. Mark Jara, the company's principal and managing director, believes the pandemic accelerated this adoption trend for prescriber engagement. Before March 2020, the predominant pharmaceutical selling model had centered around personal selling in the doctor's office. "For many brands there were months when prescriber engagement activities simply stopped while digital operations were spun up and, in many cases, reluctantly embraced," said Jara. "Tele-health tactics gained momentum and our clients made their pivot, like other industries, to fully remote operations."

While the pandemic may have accelerated an inevitable shift to certain digital platforms for activities such as tracking prescriber engagement, in other use cases it highlighted the importance of preexisting structures. For example, the number of counterfeit drugs in the American market skyrocketed over the past two years as it became more common for companies to distribute pharmaceutical products using online platforms. "The pandemic has created the perfect storm for counterfeiting as no one knew what Covid-19 related products looked like and where they would be available. It started with counterfeit test kits followed by counterfeit vaccines appearing online," explained Steve Tallant, director of market development at Markem-Imaje.

Markem-Imaje offers services including track and trace, serialization, and brand protection to help regulate supply chain security. The use of digital tools like Markem-Imaje's digital e-Fingerprint that can authenticate products anywhere along the supply chain helps combat the problem of products entering the gray market and of the sale of counterfeit drugs altogether.

Across the product lifecycle and distribution process, digital solutions are fundamental tools for success. With the advent of technology companies creating products specifically designed for the life sciences, their clients are able to adopt systems that are essentially tailor-made to help them succeed.





> The value and usability of manufacturing intelligence is at its peak during the product development process, as it enables high performance and throughput product development. Manufacturing intelligence accelerates the statistical methods utilized by traditional manufacturing by implementing nondisruptive techniques.
>
> **– Rajiv Anand, Founder, Quartic.ai**

**What can't AI do?**

Artificial intelligence has long been used within the life sciences, particularly on the clinical side to help researchers discover molecules faster. As the technology driving AI progresses, companies are finding increasingly novel ways to apply its benefits to the sector, transforming the speed and scope of what is considered possible.

One key use of AI is to help turn copious amounts of data into actionable information quickly. "The amount of data companies collect today is astounding, and we saw a need for a platform to help these companies leverage their data in a way that is fast, scalable and easy to use," said Rohit Vashisht, CEO of WhizAI, a company that offers the only augmented consumer platform currently available to life science companies in particular. "We live in an increasingly connected and on-demand world, where everybody is available online. We do not see a reason why analytics should be any different. We want users to be able to have key facts on hand in-

**Can you give an overview of AiCure and its core products?**

For 10 years, AiCure has been delivering AI to the life sciences industry to help guide data-driven decision-making for more meaningful clinical trials, optimized drug development, and improved business operations. We specialize in a deep understanding of patient behavior using phone-based video and audio. The company recently passed one million doses observed globally by our system, and we work in a variety of therapeutic areas including the central nervous system and psychiatry, infectious disease, internal medicine, and oncology.

AiCure's history is rooted in one of our core applications, Patient Connect, which is a platform for measuring adherence to medications. Patients receive an alarm through a phone app reminding them to take their medication, then our computer vision technology confirms when they have ingested it. This not only provides insight into patient behavior but also connects the patient to the clinical trial site, enabling the clinician to support the patient however necessary. AiCure's other product, Data Intelligence, mines this data to extract insights that help sponsors manage their clinical trial sites in progressing the drug.

**How does Patient Connect assist an industry-wide shift towards precision medicine?**

The collection of audio and video from a patient's own home gives insight beyond simply how people take their medicine. As such, we developed an entire arm of work around digital biomarkers. Our digital biomarker solution tracks facial expressivity, voice and speech, and general movement, then applies quantitative measures to gain insights that are more comprehensive than the data one would get from infrequent clinic visits.

We designed our digital biomarkers to be easy to use, enabling researchers to shift towards using objective quantification of behavior in their analyses through digital phenotyping. This ability to structure data collection and analyzation in a secure, compliant, and appropriate manner for clinical trials will help provide insight into how people respond to their medication over long periods of time.

**What are the limitations and advantages of this AI-based approach to tracking patient engagement?**

> We specialize in a deep understanding of patient behavior using phone-based video and audio.

## Rich Christie

Chief Medical Officer
**AICURE**

AiCure's technology allows us to approach problems in a previously unthinkable manner, bringing you into the patient's home to experience the disease in their own environment. The technology is intuitive and can capture even more than what a doctor observes and hears when sitting across from a patient.

One challenge inherent with AI, however, is the element of bias. Diversity is at our core, and we built this in from the beginning by ensuring our data training sets mirrored the potential diversity of clinical trials, from skin tone to facial hair, fingernails, and glasses. We continue to explore our model's performance to understand where we need to adapt to better serve the entire population.

**Where is AiCure currently focusing its innovation?**

We are exploring the extent to which our data can be used to develop predictive models. AiCure has already taken these steps with its dosing platform and is at a point where the platform can not only understand who is taking their medication, but also who will continue to take their medication or drop out of the trial. We are interested in expanding this towards other digital biomarkers.

**Where do you see areas of growth for AI within the life sciences space more broadly?**

AI is becoming extremely relevant in pre-clinical discovery work – being able to leverage genomic and pre-clinical data to improve the efficiency of the entire process of finding a molecule and testing it. AI is also relevant in real-world applications – understanding who is taking their medication and how they are actually responding. In this sense, we can use the power of AI to understand the real-world value of a drug and establish a strong foundation for personalized medication.

**What is AiCure's outlook for 2022 and beyond?**

We are focused on progressing our predictive platform and seeing how far we can push the ability of making our data forward-looking, both in the domain of dosing and response.

More broadly, AiCure anticipates increased adoption of its platforms. The company has noticed heightened willingness, openness, and reliance on technology to underscore participant engagement in clinical trials, and the pandemic created the need to remain in touch virtually with trial participants while making sure they are appropriately supported. AiCure's technology works perfectly to meet this need, and we anticipate that the increased adoption of our technology over the past two years will only continue to accelerate. ■





stantaneously rather than having to sift through various dashboards and reports."

Perhaps the most powerful aspect of the platform is its ability to continuously learn. Whenever a user asks a question, it further automates the system to understand context and intent, meaning that each time the product is used, by virtue of its design it improves.

Quartic.ai offers an AI solution to speed up the process of bringing drugs to market. Its edge to cloud intelligent manufacturing operations management system helps make manufacturing a more autonomous and continuous affair. While the company covers the entire drug lifecycle, it has invested more heavily into its services geared towards the early stages of product development. "What we learned from our customers is that in terms of approvals and BLS being issued, drug pipelines are accelerating exponentially. However, upon securing approval, the product development process and tech transfer manufacturing lag behind that acceleration," explained Rajiv Anand, the company's founder. "Our technology has proven to be more adoptable in bridging the gap between securing approval and the final manufacture."

According to Anand, the company has witnessed adoption rates accelerate rapidly, particularly in parallel with technologies related to RNA that progressed at lightning speed during the pandemic.

AI technology can be used in ways beyond improving operational efficiencies. In the realm of understanding patient behavior, the use of artificial intelligence may have the power to pick up on queues from people's actions even better than humans.

AiCure offers a platform that uses phone-based video and audio to produce digital biomarkers from facial expressivity, voice and speech, and general movements. From there, the solution applies quantitative measures that yield data that is more comprehensive than what would be gleaned from occasional in-person visits, according to Rich Christie, the company's chief medical officer. "AiCure's

technology allows us to approach problems in a previously unthinkable manner, bringing you into the patient's home to experience the disease in their own environment," Christie said. "The technology is intuitive and can capture even more than what a doctor observes and hears when sitting across from a patient."

Harnessing the patient's voice, both literally as achieved by AiCure and figuratively through the collection of words and statements, has become a more tangible reality. Talking Medicines is an AI-driven patient intelligence company that works to transform the voices of patients into actionable insights for pharma marketeers by gathering and sifting through immense quantities of information from social media and other forums.

Patients are empowered now more than ever by access to information. The pandemic exacerbated the tendency of people to conduct their own research online about different products on the market given the disruption towards seeing doctors in person. They found communities online in the form of support groups, shared tips and experiences, and in doing so generated copious amounts of information. Talking Medicines aims to wield this catalogue of voices into information companies can use to track the efficacy of their marketing campaigns.

According to Jo Halliday, CEO, the pharma industry spends US$30 billion annually on marketing but has shockingly low accountability for measuring returns. She believes

> The alternative means of collecting this information would be through running a research group, which has inherent bias because one person's opinion can sway the whole group. The data Talking Medicines sources is more representative because it draws from larger, disparate populations.
>
> **– Jo Halliday, Founder & CEO, Talking Medicines**

her company's platform offers the most comprehensive and organic way to gain insight into this. "The alternative means of collecting this information would be through running a research group, which has inherent bias because one person's opinion can sway the whole group," explained Halliday. "The data Talking Medicines sources is more representative because it draws from larger, disparate populations. We are also able to see if there are certain outliers, particularly a select few people who post a disproportionate amount."

From deriving actionable meaning from online support group comments to streamlining manufacturing operations, the applications of AI within the life sciences are boundless. Of course, there is still significant room for growth. "The use of AI in data analysis will expand significantly to improve early detection across a variety of diseases, as it has in oncology," posited Olga Potapova, founder, CEO and scientific director of Cureline, a global translational and precision medicine CRO that provides biobanking and laboratory services. "Unlike tech companies, however, the biomedical field has yet to fully capitalize on advances in AI and machine learning that can combine the specimens, conduct populational studies, and develop predictive models to understand the best and most economically viable approach."

According to Potapova, her company has completed over twenty large projects for companies seeking to harness the power of AI in this manner.

Overall, companies are springing up to take advantage of current industry needs, both in clinical and operational settings. This is paving the way for a world in which the use of artificial intelligence is not revolutionary, but rather expected. It is likely that within a decade we will think of companies using AI in the same way we think about how companies are harnessing the power of the internet – we do not and simply take it for granted. ■







> Tele-health tactics gained momentum and our clients made their pivot, like other industries, to fully remote operations. RxS, with our technology-forward approach, was prepared for the shift.

# Mark Jara

Principal and Managing Director
**RXS**

**How quickly did the pharma sector digitize in response to Covid-19 and how is RxS supporting the sector in this regard?**
We built our company managing prescription samples, hand delivered or shipped directly to health care provider offices, mostly through on-the-ground sales reps. As you can imagine, our clients and that selling model were immediately impacted by the pandemic. Sales representatives could not go to HCP offices. For many brands, there were months when prescriber engagement activities simply stopped while digital operations were spun up and, in many cases, reluctantly embraced. Tele-health tactics gained momentum and our clients made their pivot, like other industries, to fully remote operations. RxS, with our technology-forward approach, was prepared for the shift.

As the pandemic continued, digital platforms, like those we offer, became the tool of choice for prescriber engagement. For approximately nine months, sales reps became virtual agents and, interestingly, virtual engagement with doctors' offices continues to be a large part of the prescriber marketing solution set.

**Can you elaborate on RxS' new user-centric web portal?**
The mission behind all our digital platforms is to enable engagement, whether that engagement is between life sciences brands and their customers, sales reps and the doctors in their territories, or patients and their therapies. From the beginning, I tasked our digital marketing team to build a navigation framework that serves the needs of the visitor. To that end, the portal breaks out each component of life-science marketing and compliance with descriptions of desired outcomes and potential regulatory pitfalls.

**Can you elaborate on RxS' data processing practices and how the company turns big data into actionable information in a timely fashion?**
We process data in near real-time using advanced technologies and AI to identify and address anomalies. High-quality data, like the assets we manage on behalf of our clients, facilitates business success by enabling faster decision making -so it must be right and it must be current. Our analytics tell the whole story about the connection between sales representatives and their assigned providers, and between those providers and our client brands.

**Which of RxS' services and tools are in highest demand and driving growth for the company?**
Our non-personal engagement offerings are in high demand right now.

On the services side of the business, our healthcare dedicated contact center services have garnered a lot of interest. RxS Engage is staffed with pharmaceutical sales representatives, customer care agents, and patient services representatives. We support every phase of the product lifecycle and provide a comprehensive suite of reporting and interactive dashboards. Because these programs produce quantifiable results and positive returns on investment, they are a good bet as doctor offices consider their sales call policies.

Our digital engagement platforms, TeleTargetRx and SampleCentral, have also seen a solid uptick in demand. TeleTargetRx is our multi-channel inside sales engine – a healthcare-dedicated contact center CRM. It integrates with customer preferencing and campaign status data, enabling informed conversations that add value for HCPs and drive sales. SampleCentral, our HCP engagement portal, provides an intuitive, ecommerce-like sample shopping experience for healthcare providers. It engages them with specialized messaging, a centralized dashboard, and allocation management.

**What marketing advice would you give companies currently trying to reach their clients?**
The need to interact digitally has not only forced a change to the way brands want to interact with their healthcare provider customers, but also the way those customers wish to be engaged. The landscape has irreversibly gone digital, and the number of healthcare providers resisting that reality are dwindling.

**What is RxS' vision and objectives for 2022 and beyond?**
Our management team is betting on pharmaceutical brands stepping up their efforts to get closer to their patient-customer and their caregivers. To address that trend, we recently announced our expansion into the patient care arena with PatientCentral, a technology-enabled service that provides brands and manufacturers a single point of contact for their patients and patient caregivers.

The mission of PatientCentral is to empower brands to positively affect patient journeys and outcomes. It works through customer education and support, benefits investigation, prior authorization processing, co-pay assistance, and pharmacy triage. The RxS patient care team supplies individualized support, develops caring relationships, and ensures consistency while RxS systems track, coordinate, and report the activity of dispensing pharmacies.

The experience we have gained through our healthcare dedicated contact center, RxS Engage, makes us uniquely capable of helping patients and caregivers on their treatment journey. ■

> The pandemic has created the perfect storm for counterfeiting as no one knew what Covid-19 related products looked like and where they would be available.

## Steve Tallant

Director, Market Development
**MARKEM-IMAJE**

**How has Systech evolved since the Markem-Imaje acquisition?**
Two years ago, Systech was acquired by Markem-Imaje, a Dover Company. We had been focused on the pharmaceutical industry for over two decades with 19 out of the top 20 pharmaceutical companies in the world being Systech customers. We started as a pharmaceutical packaging execution system, with a focus on machine vison and inspection of things going through pharmaceutical manufacturing, verifying that products are properly coming off the production line. Systech got involved in pharmaceutical serialization at its germination point in the US, with California ePedigree in 2005. We then evolved with the FDA, which transformed state by state pharmaceutical regulation into the Drug Supply Chain Security Act (DSCSA). This act has had different bells to ring over the past five years with one more being implemented in 2023.

DSCSA impacts compliance needs for every pharmaceutical manufacturer in the US. Companies are required to have serialized products, and additionally, there is a salable returns requirement to validate that the products being returned are fine for resale.

Systech will remain focused on continuous innovation of our offerings, while leveraging the global reach of Markem-Imaje, with the ultimate goal of continuing to provide state-of-the-art brand protection solutions to our customers worldwide. We see the combination of Systech's solutions with Markem-Imaje's products, services and global reach enabling Systech to enhance R&D, expand global reach and provide higher levels of service to our customers.

**Has there been an increase in counterfeit drugs on the market through pandemic years?**
It is scary that the number of counterfeit drugs on the market has significantly increased over the past two years. With the pandemic, there has been a normalization of pharmaceutical distribution from online platforms, which is an easy way for counterfeit manufacturers to get their products into legitimate looking online marketplaces. Counterfeits can exacerbate health issues or even cause death.

Another important element in the pharmaceutical gray market is diverted products. Pharmaceuticals are offered at different price points based on different geographies and sometimes medicines are offered at very low costs but still must go through the legitimate supply chain. These medicines get diverted and placed into the gray market, often distributed online. There are incredibly strict supply chain realities, but once products are diverted out of the legitimate supply chain, lack of proper handling can heavily impact the efficacy of the medicine.

The pandemic has created the perfect storm for counterfeiting as no one knew what Covid-19 related products looked like and where they would be available. It started with counterfeit test kits followed by counterfeit vaccines appearing online. Governments did a good job mitigating this but could have done better informing the public that no legitimate vaccines for the Covid virus would be available online.

**How efficiently can we monitor and trace supply chains from production to pharmacy today?**
We can effectively track and trace pharmaceuticals from manufacturing or contract manufacturing to the McKesson's and Cardinal's of the world. DSCSA 2023 is really about going to the next level where we can trace and track products to dispensaries, pharmacies and doctors. The vision of DSCSA 2023 is the notion of an interoperable supply chain where any node within the pharmaceutical distribution world can be tracked and traced and we can facilitate any action and reporting we want. The model is based on aggregated serialization where, for example, if you have a serialized 'each', it gets placed into a serialized case, which then gets placed on a serialized pallet, and with one scan of the pallet at a distribution center everything moves in tandem. The Systech team is participating in a group called the Partnership for DSCSA Governance (PDG) where it is in an ongoing buildout of what the entire interoperable supply chain looks like from a technology standpoint.

**How do different country regulations impact the traceability of drugs?**
At the end of the day, it's all the same, but slightly different. It's about having a serialized product, individually identifiable, with the data available—for the intended market. The difference in regulations from country to country is the openness of the data. For example, the EU Falsified Medicines Directive (FMD) requires the serial number to be validated when it is manufactured and then only again when it is dispensed. There are many things that can happen throughout the pharmaceutical supply chain between manufacturing and dispense. The US FDA recognized this and is thus implementing a regulation where products are tracked and traced throughout the entire supply chain.

**What is Systech's vision for growth for 2022 and beyond?**
First is ensuring our Systech customers are compliant with DSCSA 2023 regulations. Second, while serialized barcodes on packages have a digital component, they are essentially printed elements that can be copied, fabricated and reproduced. With our vision technologies and expertise, we are able to create a double layer of product protection. ■





## Rohit Vashisht

Co-Founder & CEO
**WHIZAI**

**Who are WhizAI's target clients?**
Our strong suit is commercial pharma, and we are advancing in manufacturing, supply chain, clinical R&D, and recently patient services. We recently found success with Medtech companies and are now expanding to payers and providers, helping customers in the US and Europe.

**Are patients able to witness benefits from these tools firsthand?**
While patients do not interact directly with WhizAI tools, people in pharma who impact the patient experience absolutely do. For example, people within patient service roles at big pharma companies see clear benefits by providing a holistic view of the entire patient journey through each step of the process, with real-time Insights, from referral through titration and adherence. Here, the benefit is how instantaneously users can get the lowest-level details to then figure out what is happening in a unique situation. From a patient's perspective, what used to take days can now happen quickly, improving their overall experience and potentially their health outcomes.

**What role do you see AI playing in the life sciences over the next few years?**
Although AI is relatively new today, in 10-15 years every application will be AI-enabled. I see a lot of room for advancement within certain IoT applications in which it is humanly impossible to track all the data. Additionally, there is a lot of unstructured data in the form of patient or doctors' notes, and we see a tremendous potential to apply AI towards molding this into actionable information. On the clinical side, AI enables researchers to discover molecules faster.

**How do you see WhizAI growing in the near term?**
WhizAI is just getting started. We started the company only five years ago and are now seeing large pharma adopting our platform, trusting it to run their analytics. This is a testament to how hungry our customers are for companies that offer products like ours.

I anticipate we will double the size of the company by the end of 2022, and we are on track to do 300% revenue growth in the same timeframe. ■

## Rajiv Anand

Founder
**QUARTIC.AI**

**Could you remind our readers about Quartic.ai's mission?**
Quartic.ai's mission is to enable autonomous and continuous manufacturing, especially for biopharma, to accelerate the speed with which drugs are brought to market. We provide a complete edge to cloud intelligent manufacturing operations management system that can be utilized for different manufacturing industries, particularly those that are heavily regulated. The life sciences is our most important industry vertical and represents 60-70% of the company's focus.

**Where in the manufacturing process do Quartic.ai's systems have the most impact?**
We focus on early-stage manufacturing, meaning product development and CMC. In terms of approvals and BLS being issued, drug pipelines are accelerating exponentially. However, upon securing approval, the product development process and tech transfer manufacturing lag behind that acceleration. Our technology has proven to be more adoptable in bridging the gap between securing approval and the final manufacturer. While we continue to cover the entire drug lifecycle, we have invested more in those early stages of product development, which underscores the industry shift towards an increased reliance on CDMOs and effectively aligns the sponsor of the molecule with the manufacturer or developer.

**Can you elaborate on why Quartic.ai's AI platform is most applicable to product development?**
The value and usability of manufacturing intelligence is at its peak during the product development process, as it enables high performance and throughput product development. Manufacturing intelligence accelerates the statistical methods utilized by traditional manufacturing by implementing nondisruptive techniques, such as Bayesian experimental design, a tool to help guide experiments based on a probability-theoretical framework that interprets data throughout the experiment. Moreover, deploying these techniques in the early stages renders AI adoption easier, as one has already transferred that knowledge algorithmically. ■

# Concluding Thoughts

***The US life sciences industry presently faces a host of challenges and opportunities for growth. As a broad-reaching ecosystem with immense diversity in its actors, these trends are inherently diverse. The following selection of quotations highlights voices discussing a variety of the most pressing topics currently impacting the life sciences. We thank the individuals who took the time to share their insights with us, and we look forward to continuing to learn from them in the years to come.***

"AI is becoming extremely relevant in pre-clinical discovery work – being able to leverage genomic and pre-clinical data to improve the efficiency of the entire process of finding a molecule and testing it. The use of AI to optimize how clinical trials are executed has tremendous potential in the years to come, as it gives us a lens into how the mechanics of the trial are going."

**- Rich Christie, Chief Medical Officer, AiCure**

"Over the last two years, we moved swiftly from conventional mRNA to self-amplifying mRNA, as opposed to each one taking 10 years to develop and implement. We hope the self-amplifying mRNA will be a more durable vaccine with broader variant coverage, which is desirable as we transition into an endemic booster market."

**- Joseph Payne, President & CEO, Arcturus Therapeutics**

"All the polling numbers show that patients care primarily about reducing their out-of-pocket costs. Any development must start at this point, focusing on reducing costs for buyers while still making a return for their investors through delivering a value-add to the market. The best way to do so is to leverage innovative technology that increases operational efficiency."

**- Edward Allera, Co-Leader – Life Sciences Industry Group, Buchanan Ingersoll & Rooney PC**

"We see a trend in the ownership of the development pipeline and commercialization of new products shifting from large pharma to small and mid-size companies. This has driven an increased level of outsourcing, as smaller companies tend to need more support along the development journey and often own no commercial-scale manufacturing assets. CDMO outsourcing rates are still relatively low, roughly 40-50% depending on the service, and we expect that rate to continue to grow."

**- Thomas Loewald, CEO, Cambrex**

"From a public company perspective, credibility is critical, and we are seeing this even more so in the venture capital community. At the early stage of investment, if you are not able to secure a significant venture capital round it will be very difficult to do so at a later stage. If you do not have the inside track from the beginning, it is hard to get there as there is a significant volume of companies with interesting ideas, and investors are going to the sources they feel are most likely to succeed."

**- John Pennett, Partner-in-Charge of the National Technology and Life Sciences Group, EisnerAmper**

"We have seen a huge influx of capital into the life sciences sector during 2020 with generalist funds and public funds investing in early-stage healthcare. The limiting factor has not been capital, but talent in the marketplace. We are now seeing a 'hangover' effect in the market with the XBI still down; valuations are starting to return to normal as expectations to finance for the long term are again receiving priority."

**- Lori Hu, Managing Director, Vertex Ventures HC**

"While we definitely see reshoring of manufacturing, we do not see it as much for discovery services. If you have an eight-step synthesis, perhaps only the final two steps are moving back to the US. "

**- Manni Kantipudi, Chief Executive Officer, Aragen Life Sciences**

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