

the Medicine Maker

BIOPHARMA
TRENDS 



LEADERS' REPORT 2022



FOREWORD

Delving into the Trends of the Biopharma Industry



What a three years it has been... It was business as normal in December 2019. By March 2020, a number of western countries had “locked down.” No one was prepared. Those first few months were a surreal and uncertain experience for us all. As a key industry, biopharma had to carry on – learning how to operate facilities in a COVID-19 safe way and navigate fragile supply chains. Many clinical trials were halted, but other companies forged ahead with planning and undertaking trials to test potential COVID-19 vaccines. By the end of 2020, vaccines were being administered.

That is remarkable.

Fast forward to 2022 and, in many countries, life is back to some semblance of normality, but the world has changed. Biopharma has changed. There is broad acknowledgement that supply chains are not quite good enough. The industry collectively knows that it must be

ready for the next crisis. But, perhaps most of all, we recognize that the lessons learned during our fight with COVID-19 must be applied to other therapeutic areas. We need to bring new drugs to patients faster – and COVID-19 has proven that it can happen.

Departing from our traditional survey based report, Biopharma Trends 2022 explores the views of leaders from across the biopharma industry in a series of exclusive interviews. Here, we present the resulting selection of thoughts and insights into the trends that will shape biopharma in the coming years – from accelerating R&D in mRNA therapeutics and pushing the frontiers in cell therapy to finding new ways to deal with the increasingly competitive environment for talent.

Stephanie Sutton
Editor, *The Medicine Maker*

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Maik Jornitz, CEO, G-CON Manufacturing

KEY THOUGHTS

“Supplies were pressured to such an extreme that it became critical for the end-users to validate new equipment suppliers into their manufacturing process, which is a difficult and lengthy undertaking.”

“SARS, MERS, and H1N1 all gave us a taste of the true threat of viral diseases, but after a short period of hype for ‘doing something about it,’ all the initiatives fizzled out.”

“Processes and facilities do not need to be constantly reinvented; when standardized, they can be cloned. Cleanroom infrastructures can be mass produced as products instead of being built as complex, manual, on-site projects.”

What changes have been ushered in by the COVID-19 pandemic in the biopharma industry overall?

From the facility viewpoint, the pandemic introduced two new factors. Firstly, during the pandemic it became obvious that capacity implementation must be carried out much faster and more flexibly, as process design can vary with new therapy developments. Secondly, off-site modular facility construction benefited from not being interrupted by pandemic lockdowns.

Both factors have underlined the importance of speed and flexibility to shape a “new normal” in facility design and construction. From-scratch design and build project execution has become obsolete and

undesirable because it is too slow to serve the new needs of faster capacity implementation. This “new normal” does not ask for 2–3 years to construct a manufacturing site. Instead it installs one in 6–12 months, with the construction and prequalification performed off-site.

In the area of process equipment, we have seen major stress inflicted on the supply chain, especially in single-use process technologies. Supplies were pressured to such an extreme that it became critical for the end-users to validate new equipment suppliers into their manufacturing process, which is a difficult and lengthy undertaking. Again, these pressures created another “new normal” and pushed end-users to the realization that new technologies can be introduced into existing processes when necessary.

What are the most exciting advances in terms of vaccine technologies and manufacturing processes?

The development of mRNA treatments accelerated – not only from a research and process development standpoint, but also in terms of regulatory review and oversight. The acceleration of research and development for mRNA vaccines has also opened the doors for new therapeutic research. It is very encouraging to see that mRNA will not only be explored for COVID-19 vaccines, but also for flu and for oncology treatment options. Our hope must be that mRNA therapies will support the development of a broader scale of vaccine treatments, including for diseases that do not yet have a vaccine.

Post-pandemic, how do you think activity around vaccines will change? Will it drop back to normal levels or will vaccines still be a key focus point?

The focus on vaccines and vaccine technologies cannot diminish or return to normal levels because the pandemic showed us just how utterly unprepared we were. The hope has to be that the global community looks into preparedness and protection against new, upcoming viral entities. The COVID-19 pandemic is far from over – and again a “new normal” has fallen into place.



Vaccines must evolve alongside the evolution of the COVID-19 viral entity, and with the rise of new infectious diseases. The general lack of motivation to invest into pandemic preparedness prior to COVID-19 should concern us all.

SARS, MERS, and H1N1 all gave us a taste of the true threat of viral diseases, but after a short period of hype for “doing something about it,” all the initiatives fizzled out. I find it incomprehensible that the developed world is still not investing in capacities that can be deployed at a moment’s notice. Such a capacity would cost, say, US\$100-200 million, which would be nothing compared with the lives saved and reduction of the subsequent economic downturn. Too often, realistic activities are drowned in red tape and unproductive discussions. Besides the unpreparedness in the developed world, there is no true plan for a global equitable vaccination program. We need to deploy small scale vaccine manufacturing units. These units have existed for 10 years, but again traditions overrule innovations and patients do not get treated.

What types of biopharmaceutical products do you think will be the most important in the coming 5–10 years?

The most important therapies entering the field are cell, gene, and mRNA therapies. All of them can be highly targeted and demonstrate considerable efficiencies against cancer and rare diseases. What could not be treated in the past is now treatable. We must hope that in future we can treat cancer with vaccines, or at least using means much more targeted than the “atomic bomb” of chemotherapy.

Cell, gene, and mRNA treatments are still in their infancy. Over the next five years, we will see their potential. Older treatments will be replaced by newer, safer, and more effective treatment options. Five years ago, I saw a video about the vision of the Mary Crowley Cancer Research Institute in Dallas, which discussed the possibility of checking the entire genetic profile of a patient, understanding the potential cancer markers, and treating these immediately with a

vaccine. This bold vision now seems more and more a possible reality or at least we need to hope for it.

What are the biggest challenges when it comes to bringing new products to market?

The biggest challenge is the industry itself – and beliefs that the old and the inefficient are better than the new and the innovative. It is well known that the biopharmaceutical industry is deeply inefficient, mainly because radical changes in the thought and action of the industry only happen when they are absolutely necessary – or when early adopters prove that the gain in efficiencies are so outstanding that these early adopters become major competitors. Nobody wants to be the first, but everybody wants to be the fastest second.

We can see an excellent example of such behavior in the implementation of single-use process technologies. It took 20 years for single-use to become the go-to technology, because the majority of end-users stuck to stainless steel. Their thinking was that a one-off investment into steel equipment would be the end of all costs, not realizing that the cleaning, steaming, and set-up of steel equipment results in much higher operating costs than those of single-use. When the far superior performance of early adopters made this fact impossible to ignore, single-use technology went mainstream.

What areas of biopharma manufacturing should be a priority for future innovation and why?

Ultimately, every player in supply, regulation, and industry works for the patient!

Therefore, the focus has to be on “the patient” at large, and not just the patient who can afford the medicine. And that means we must look to patient-focused investment, biomanufacturing economics, and supply optimization. Why are large glass palaces still built, previous designs redesigned, everything customized, and projects made artificially

complex? Is it simply to satisfy hourly rates or does a beautiful building create higher shareholder value?

Meanwhile, other industries are constantly striving for speed and efficiency. This is because they understand their end-customer, the consumer, will turn away from them if costs and availability are not optimal.

It is time for a rethink. We must change (or at least embrace the basic concept of change) to determine what is possible, and how efficiencies and cost savings can be achieved using what is available. Processes and facilities do not need to be constantly reinvented; when standardized, they can be cloned. Cleanroom infrastructures can be mass produced as products instead of being built as complex, manual, on-site projects. Entire sites could be designed as turnkey solutions, available in turnkey solution catalogs for every possible application, facilitating speed, certainty and repeatability.

What are the biggest challenges (for pessimists) or biggest opportunities (for optimists) when it comes to the growth of the biopharma industry?

Typically, the pessimists point at the regulators. But as regulators become more and more open to discuss and learn, this excuse is losing its staying power.

I do not mean to deny we are working in a highly regulated industry. We are. But so are others, and they still implement far more innovations than us. The challenge in our industry is that the known shall not be challenged; a fairly apathetic, if not selfish viewpoint. There is always new technology on the horizon able to enhance our processes and facilities, and these should be enthusiastically implemented rather than disparaged and delayed.

The biggest opportunities are the new therapies; they are designed by creative people, and require new technology and implementations. This combination of the open mind and the thinking of infrastructure will accelerate change, efficiency, and safety.

Mike Thien, Senior Vice President, MSD

KEY THOUGHTS

“Certainly, the excitement associated with the mRNA platform itself cannot be denied, but we should not overlook the willingness of regulatory agencies to facilitate acceptance of this new platform.”

“More than ever, developers must not only ask ‘will this be safe and efficacious,’ but also ‘will this be reimbursable, and at what rate and where?’ before deciding to go forward with new product development.”

“We currently face an extremely challenging environment, not only for recruitment but for retention as well. Though there are no sustainable solutions yet, there are some approaches that have yielded positive results.”

What changes have been ushered in by the COVID-19 pandemic in the biopharma industry overall?

The COVID-19 pandemic has certainly changed how we look at the manufacturing process. Given shortages, supply chain challenges, cold chain capacity, and secondary impacts on supply, warehousing and distribution, “end-to-end” considerations have expanded from the process and its direct consumables to include in-depth looks at supply chains (including the suppliers of our suppliers and beyond). More consideration will be given

to future adverse scenarios, inducing better “future-proofing” as technology platforms, site selections, distribution networks and digitization are considered. It is also likely we will see better running tallies of available global capacities and capabilities kept by international groups involved in emergency response (the WHO, CEPI, Gates, and so on).

What are the most exciting advances in terms of vaccine technologies and manufacturing processes?

While living under the present undesirable circumstances, it is indeed reassuring that there is now a much more widespread appreciation of vaccines and their related technologies and processes. It is to be hoped that more dollars and thought will be spent investigating new technologies in the vaccine manufacturing arena. Certainly, the excitement associated with the mRNA platform itself cannot be denied, but we should not overlook the willingness of regulatory agencies to facilitate acceptance of this new platform. Another exciting advance is the seriousness with which globally distributed vaccine manufacturing capacity (for both antigen production and for downstream operations, form/fill and packaging) is being discussed, and in some cases, already utilized.

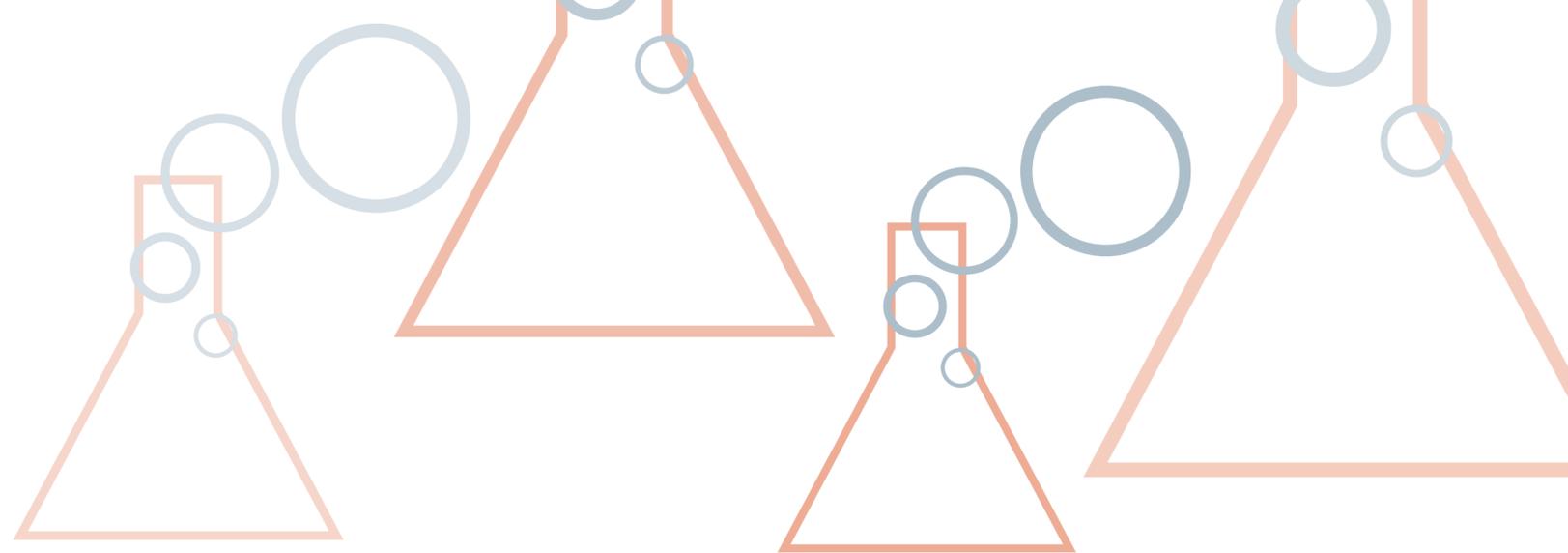
Post-pandemic, how do you think activity around vaccines will change? Will it drop back to normal levels or will vaccines still be a key focus point?

We expect a variety of post-pandemic responses in the vaccine arena. As the pandemic eases, it is likely that the general public will revert

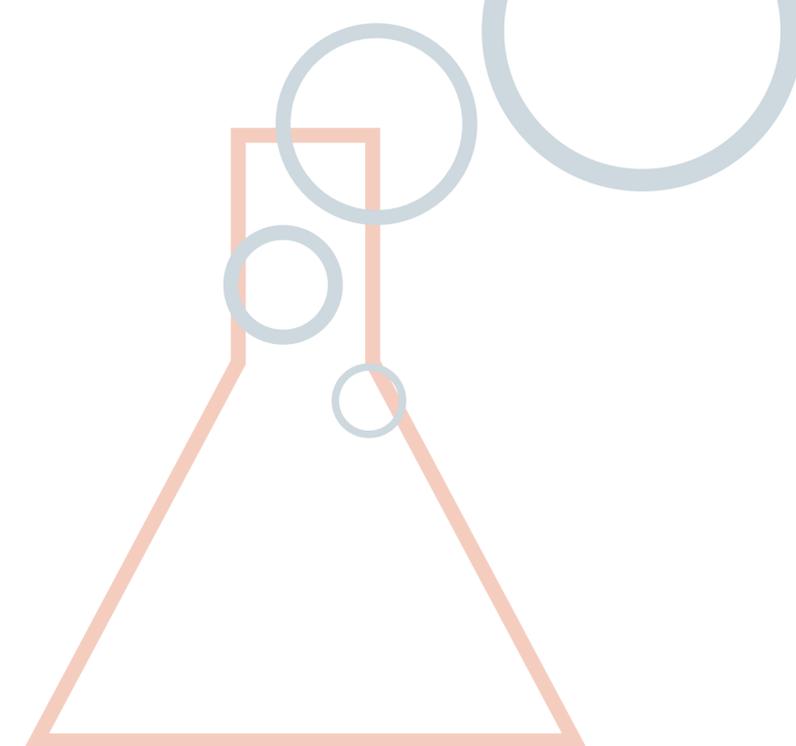
back to a lesser concern or awareness of vaccines, but with the new assumption that it will be possible to develop and deploy vaccines against future pandemics in similar timeframes. It is also likely that funding for vaccine work, both private and government, will similarly recede. On the other hand, vaccine mandates have hardened, added to the “anti-vax” movement, and could lead to more resilient and active anti-vax activities. There is also likely to be significant pressure from governing bodies worldwide to push for localized/national vaccine manufacturing capabilities.

What types of biopharmaceutical products do you think will be the most important in the coming 5–10 years?

As our understanding of underlying biology increases every day via the advent of new tools and the use of AI, we will have increasing call for and capability to deliver more personalized/individualized medicines, including bespoke gene/cell therapies and population-directed medicine based on biomarkers and genetics. Though the latter can take advantage of the many currently existing platforms (small molecules, monoclonal antibodies, traditional vaccine platforms), the nascent and industry-disrupting cell/gene therapy platforms will straddle both bespoke therapies and larger population therapies for unmet medical needs. In addition, synthetic biology, advances in conjugation technology, and an improved ability to make much larger molecules synthetically will also deliver new platforms. Regardless of type, all of these new platforms will face the same pressures as existing platforms: the challenge by payers and governments to spend less per patient and seek substantially lower prices for effective new therapies.



“Certainly, the excitement associated with the mRNA platform itself cannot be denied, but we should not overlook the willingness of regulatory agencies to facilitate acceptance of this new platform.”



What are the biggest challenges when it comes to bringing new products to market?

With science advancing at unprecedented rates, it would appear that innovation is not the rate-limiting step for new product introductions. Risk tolerance/aversion, an unharmonized global regulatory system, the increase in number and diversity of health technology assessments, and pricing create challenges for new product introduction. More than ever, developers must not only ask “will this be safe and efficacious,” but also “will this be reimbursable, and at what rate and where?” before deciding to go forward with new product development and commercialization.

What areas of biopharma manufacturing should be a priority for future innovation and why?

Challenges for manufacturing platform selection are many. Technological choices need to address sustainability, religious (kosher, halal) and moral (use of human-hybridized cells) constraints, raw material and consumable supply chain considerations (shortages, diversion to greater need), and distribution supply chain considerations (cold chain capacity). And, of course, cost is becoming an increasingly important factor.

In the small molecule arena, sustainability of processes needs to be a chief concern, and thus enzymatic synthesis, photochemistry, and other renewable platforms must be further developed. For biologics and vaccines, productivity (intensification and continuous manufacturing) and careful consideration of process inputs and product components must be a priority. Considerations for product thermostability must be more vigorously emphasized during initial product selection. And, given the learnings from the pandemic, supply chain robustness and greater market responsiveness must be kept in mind when selecting manufacturing facilities, equipment, and components.

What are the biggest challenges (for pessimists) or biggest opportunities (for optimists) when it comes to the growth of the biopharma industry?

The challenges are apparent, chief of which is pricing/access, and then the sustainability and responsiveness of our offerings. But we are not without opportunities. Global regulators have shown a willingness to accept new platforms, the pandemic has given rise to increased harmonization across regulators, and there are an increasing number of opportunities for the industry to work together with global organizations (for example, the WHO and CEPI) for the

common good. The ability to address these challenges and seize these opportunities, coupled with the advances in science, offers the means to transform our industry.

How challenging do you find workforce recruitment and development? And what best practices would you recommend to address this challenge?

We currently face an extremely challenging environment, not only for recruitment but for retention as well. Though there are no sustainable solutions yet, there are some approaches that have yielded positive results.

Investment in feeder pools (secondary and post-secondary education and vocational training) have been shown to increase the number of applicants seeking employment in our industry. Many are experimenting with new programs to address the needs expressed by the new hire demographic. These include alternative pathways for broader roles with faster rotations (including those across modalities) and alternative work arrangements. We have yet to see the full impact of changes brought about by the pandemic, but it is very likely that work practices will have to be adapted (to favor more hybrid work arrangements) and maintained well after the pandemic has ended.

Jan van de Winkel, President & CEO, Genmab

KEY THOUGHTS

“One of the biggest challenges is the question of how long it can take for medicines to progress from initial concept to launch, given the lengthy research and development process.”

“Regarding manufacturing for our pipeline of modified antibody candidates, we have found great value by working with CMOs, who now offer specialized one-stop-shop services to support the manufacturing of these advanced antibodies.”

“There are plenty of opportunities for growth in the biopharma industry, but what excites me most are the cross-industry partnerships that can potentially facilitate the next big breakthrough. We understand that innovation cannot happen in a vacuum.”

What changes have been ushered in by the COVID-19 pandemic in the biopharma industry overall?

Throughout the pandemic, we saw the biopharma industry come together and collaborate on an unprecedented scale. We've always believed that collaboration is essential to accelerate innovation and transforming cancer therapies for patients, but this past year presented

additional challenges, so it has been important to leverage expertise and technology to assist with efforts against the pandemic.

As an example, our scientists worked with a private research institute in the Netherlands to develop a robot that could perform large-scale PCR testing, processing up to 20,000 samples in 24 hours. This work enables diagnostic testing for COVID-19 and other infectious diseases on a massive scale. It was one of several industry examples of partnerships helping to meet societal needs.

I expect to see more cross-industry collaborations in the near future, between players such as biotechnology companies, research institutes, technology companies, and big pharma.

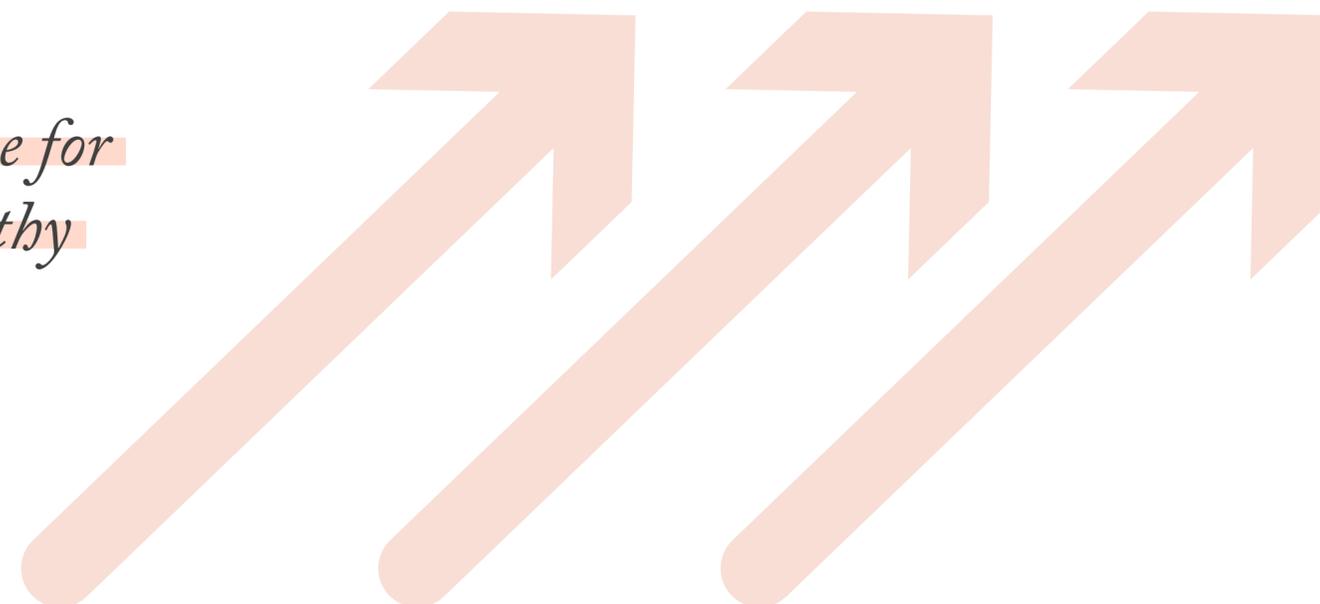
What types of biopharmaceutical products do you think will be the most important in the coming 5–10 years?

We believe that therapies able to make an impact on the lives of patients with difficult to treat conditions will be important. We are excited about the pace at which science and technology are moving us toward meeting these patients' needs, but there remains much to do.

I see a focus on human antibodies to treat various types of cancer. Bispecific T-cell engagers, next-generation immune checkpoint



“One of the biggest challenges is the question of how long it can take for medicines to progress from initial concept to launch, given the lengthy research and development process.”



modulators, effector-function-enhanced antibodies, and antibody-drug conjugates could also play a role for cancer patients.

What are the biggest challenges when it comes to bringing new products to market?

One of the biggest challenges is the question of how long it can take for medicines to progress from initial concept to launch, given the lengthy research and development process. That said, we believe in the power of next-gen technologies to enable innovation and help medicines reach the patients who need them.

What areas of biopharma manufacturing should be a priority for future innovation and why?

We have seen biopharma manufacturing develop immensely in recent years. Regarding manufacturing for our pipeline of modified antibody

candidates – which includes bispecific T-cell engagers, next-generation immune checkpoint modulators, and antibody-drug conjugates – we have found great value by working with CMOs, who now offer specialized one-stop-shop services to support the manufacturing of these advanced antibodies.

What are the biggest challenges (for pessimists) or biggest opportunities (for optimists) when it comes to the growth of the biopharma industry?

There are plenty of opportunities for growth in the biopharma industry, but what excites me most are the cross-industry partnerships that can potentially facilitate the next big breakthrough. We understand that innovation cannot happen in a vacuum, so we have partnered with various organizations – including biotech and pharma companies, academia, research institutes, and data science businesses – to create a robust innovation ecosystem. For example, we have

combined our insights with Tempus' AI tools to research novel disease targets and advance new treatments in oncology. Currently, we are engaged in a collaboration with the Princeton Catalyst Initiative (PCI) to unlock approaches in translational cancer research, antibody science, and data science. These partnerships have the potential to advance meaningful treatments for patients, and we are looking forward to seeing what we can achieve together.

How challenging do you find workforce recruitment and development? And what best practices would you recommend to address this challenge?

Companies must pursue the best talent, but it's an exciting time to join a biopharma because of the potential positive impact you can have on patients' lives. A good company should be committed to ensuring an inclusive workplace that prioritizes people, and ensures everyone is respected, heard, and appreciated.

Amélie Boulais, Manager of Market Entry Strategy, Separation Technologies, Sartorius

KEY THOUGHTS

“In some cases, there may be no need for a dedicated facility. Drug developers can make use of flexible platforms, in flexible facilities, relying on single-use technologies. I believe that the vaccine facility of the future could be a ballroom concept.”

“One of the biggest opportunities for me is the rise of new modalities: gene and cell therapies, mRNA, exosomes, gene editing...”

“We are witnessing a significant shortage of specific skills and experience in the labor force for the biopharma sector.”

What changes have been ushered in by the COVID-19 pandemic in the biopharma industry overall?

I do not think that a massive change has been ushered in by the pandemic, but existing trends have been accelerated during the crisis. For instance, single-use technologies, which have been widely adopted in the industry over the past decade, proved crucial for the production of COVID-19 vaccines and the rapid ramp up in global vaccine production capacity. The pandemic has also accelerated existing conversations around strong supply chains and standardization in, for example, the design of single-use assemblies.

The pandemic has also put new modalities into the spotlight – such as mRNA or viral vectors – and attracted new investors. The first approved mRNA therapeutic is an mRNA vaccine, but the potential goes beyond a prophylactic vaccine. Think protein replacement, cancer immunotherapy, gene editing... investment in the field has boomed since 2020.

As a final thought, digitalization trends have also accelerated. Digital transformation to accelerate innovation, such as the use of artificial intelligence to identify drug candidates or improve process efficiency, and the use of big data to support continuous processing was already underway. The COVID-19 pandemic took digitalization further, with all of us having to digitalize human interaction too.

What are the most exciting advances in terms of vaccine technologies and manufacturing processes?

The rise of mRNA is probably the most exciting and visible advance in the field of vaccination, thanks to flexibility and speed of development and production. The mRNA vaccines were first to market for COVID-19, while demonstrating excellent efficiency. mRNA has now become an essential weapon in the vaccine developer's toolbox. Together with viral vectors, mRNA vaccines are proving that vaccines can be made with a platform approach.

In the past, the vaccine industry relied on traditional vaccines manufacturing (i.e., inactivated or attenuated processes), meaning we had to develop a process tailored to each disease – one bug; one drug. Going forward, I think we will see the vaccine industry relying on a network of CDMOs to produce clinical material and start commercial production before investing in a dedicated facility. In some cases, there may be no need for a dedicated facility. Drug developers can make use of flexible platforms, in flexible facilities, relying on single-use technologies. I believe that the vaccine facility of the future could be a ballroom concept.

Post-pandemic, how do you think activity around vaccines will change? Will it drop back to normal levels or will vaccines still be a key focus point?

There is clearly a peak of activities now, but the intensity of research



and investment around vaccines will likely decrease in the coming years. Some lessons learned from the COVID-19 crisis will impact future vaccine development:

- The vaccine pipeline is more diversified, with new approaches that can accelerate time to clinic.
- Collaboration between different stakeholders (developers, producers, public institutes, regulation bodies) can support the development of vaccines against unmet indications or pathogens with a high pandemic risk. We can expect more investment for these indications, which will hopefully support readiness for the next crisis.
- Local production of vaccines is critical to ensure global access to vaccines, especially in a pandemic situation. Some countries, such as China, have been able to bring their own vaccines to market very quickly. I expect to see more governments investing in local capacity to produce vaccines.

What types of biopharmaceutical products do you think will be the most important in the coming 5–10 years?

It is difficult to predict which type of biopharmaceutical will become the most important. Monoclonal antibodies have proven their value; cell and gene therapies have been rising for a few years; mRNA-therapies have just made it to the market; exosomes are on the watch list... I believe all of these will be important over the next 5–10 years (depending on clinical trials for the newer approaches) – and it's important to have a toolbox of therapeutics for first-line and second-line treatments.

If we look at cancer treatment today, chemotherapy or radiation are often the first-line treatment, while mAbs or even CAR-T therapies can be considered second-, or third-line treatments. The rise of one biopharmaceutical product does not eclipse other lines of treatment.

I see the same trend in the vaccine industry. Although mRNA

vaccines have been successful for COVID-19, they might not be the best fit against other pathogens. The future will tell us what the sweet spot for mRNAs is.

What are the biggest challenges when it comes to bringing new products to market?

CMC is probably one of the biggest challenges for new types of modalities. These products often target rare diseases, meaning they follow expedited approval tracks. Companies can face delays in bringing their products to clinics if they are not properly prepared. All products need to be developed with the aim in mind from the very beginning to properly identify CPPs and CQAs.

I believe that the lack of consistency in testing product quality can lead to delays in approval. Testing can be a challenge when evolving a new field for three reasons: i) when the analytical solutions are laborious, time consuming; ii) when the processes are variable; iii) when the regulatory landscape is evolving over time, while the industry is still on the learning curve. Developers can mitigate risk and build a solid process understanding by implementing high-throughput technologies, orthogonal analytical solutions, and the right data analytics solutions.

What areas of biopharma manufacturing should be a priority for future innovation and why?

As current biological product pipelines become more diverse, product demand and cost pressures are increasing. To meet these demands, manufacturers often move towards process intensification. By making changes to unit operations, to the process, or even to the type of facility, the industry can identify areas of potential improvement that can increase productivity, reduce timelines, downsize process footprint, and lower cost of goods. But there is a massive amount of information to consider when performing process intensification, which adds to the already complicated nature of biomanufacturing and its unique regulatory challenges.

What are the biggest challenges (for pessimists) or biggest opportunities (for optimists) when it comes to the growth of the biopharma industry?

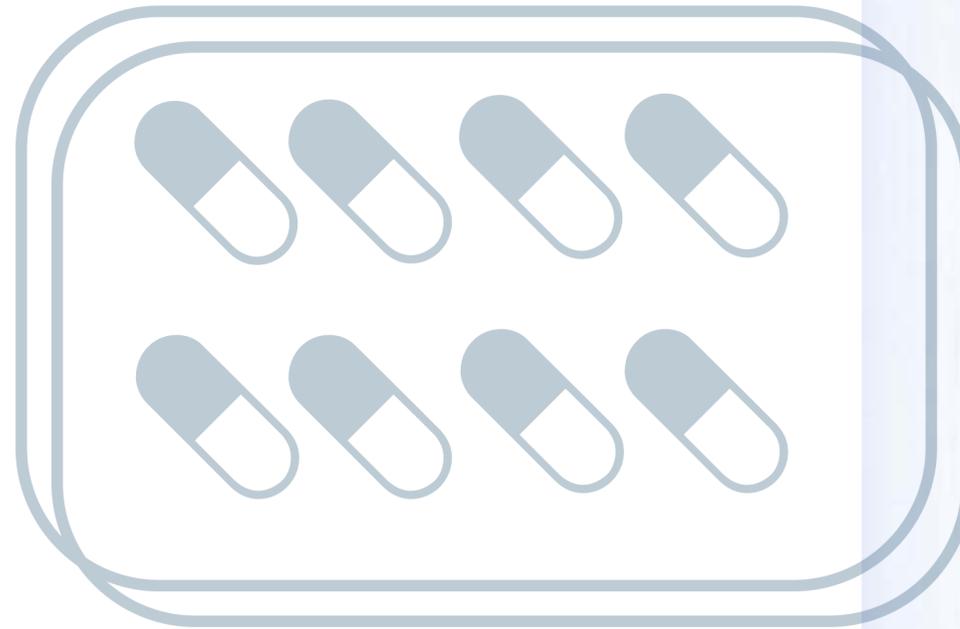
One of the biggest opportunities for me is the rise of new modalities: gene and cell therapies, mRNA, exosomes, gene editing... They hold a lot of promises for unmet indications, and the outcome of clinical trials in the coming years will give us a better understanding of the sweet spot of these new modalities. However, they also raise questions and bring challenges:

- How do we establish robust and effective CMC and analytical strategies in a new and evolving field?
- How do we scale up to meet demand, at an affordable cost?
- Supply chain issues: mRNA therapies have put the spotlight on raw materials. The sudden boom of mRNA vaccines created bottlenecks in the supply of raw materials, such as enzymes. The industry will have to ramp up capability to cope with the demands that are specific to these new products.

How challenging do you find workforce recruitment and development? And what best practices would you recommend to address this challenge?

We are witnessing a significant shortage of specific skills and experience in the labor force for the biopharma sector, especially in niche or developing therapies, such as cell and gene therapies, mRNA, and so on. But CDMOs are poised to help extend customers' workforce by providing experts in specific applications and technical areas. Some CDMOs also provide customers with training or other learning opportunities so that they can extend the skills of in-house staff and bring the latest and greatest technology to their teams. I think biopharma manufacturers have to look at suppliers as collaborators to help bridge some of the resource gap they're experiencing. Working together, we see our relationship transform from that of customer and supplier, to one of mutual support and benefit, with the goal of simplifying progress for the industry.

James Morton, Associate Director, Manufacturing/ Industry 4.0 and Chris Meier, Managing Director and Partner, Boston Consulting Group



James Morton



Chris Meier



KEY THOUGHTS

“The understanding and recognition of the importance of vaccines has grown and this should impact the share of healthcare spend going forward.”

“I think the shift to more personalized, biomarker-driven medicines derived from genomic data will be core to the growth in the sector.”

“Lower costs, ease of administration, and better product stability are all important to improve global access.”

What changes have been ushered in by the COVID-19 pandemic in the biopharma industry overall?

We have seen a huge acceleration in terms of digital ways of

working, from R&D to clinical practice. Lead-times for vaccine development and approval that were unheard of pre-COVID-19 – as well as decentralized trials, virtual visits and telemedicine – have all transformed medicine end to end. From a manufacturing perspective, there has also been a significant increase in the adoption of digital capabilities, including remote assistance, remote tours, use of video footage for audit, and remote tech transfer.

What are the most exciting advances in terms of vaccine technologies and manufacturing processes?

The development and approval timelines for vaccines is the big game changer here – and shows the potential of what can be achieved when regulators and industry work together for patient outcomes. This fundamentally improves the provision and availability of vaccines for tackling global illnesses.

In my view, the use of biological process digital twins to match the pace of innovation is another positive shift seen in manufacturing.

“The understanding and recognition of the importance of vaccines has grown and this should impact the share of healthcare spend going forward.”



Post-pandemic, how do you think activity around vaccines will change? Will it drop back to normal levels or will vaccines still be a key focus point?

Disease prevention has found its moment in the spotlight, and I see great opportunity here. The understanding and recognition of the importance of vaccines has grown and this should affect the share of healthcare spend going forward. The fundamental shift in the way vaccines are developed, trialed, and approved will be a lasting impact from the pandemic

What types of biopharmaceutical products do you think will be the most important in the coming 5–10 years?

We have already seen a tectonic shift away from small molecules to biologics. This trend will continue with the addition of even more promising technologies, such as ADCs, cell therapies, and RNA-based vaccines. In all of this, I think the shift to more personalized, biomarker-driven medicines derived from genomic data will be core to the growth in the sector.

What are the biggest challenges when it comes to bringing new products to market?

First and foremost will be demonstrating the unique value to patients, which, in the coming years, needs to include a wider set of patient populations. It will be a huge challenge to identify and recruit more diverse patient populations into clinical trials as well as leveraging real world evidence to show where impact is really happening.

What areas of biopharma manufacturing should be a priority for future innovation and why?

In newer modalities, the move towards more personalized medicine presents a significant challenge for manufacturers, driving a step change increase in complexity, on relatively manual processes. A push towards decentralized production and the inevitable pressure on vein-to-vein time to deliver required outcomes add to this challenge.

Improving manufacturing and supply chains to make them better, smarter, and cheaper will contribute to improving access to medicines for all – and

that’s particularly true for biologics, where improving global access will be key for the future of the industry. Lower costs, ease of administration, and better product stability are all important to improving global access.

What are the biggest challenges (for pessimists) or biggest opportunities (for optimists) when it comes to the growth of the biopharma industry?

Reducing the failure rate in innovation is the biggest lever to driving growth in the sector. Doing so will translate directly into value for the patient, growth opportunities for companies, and fuel further investment in innovation. Harnessing the increasing wealth of omics data and the massive power of AI and machine learning will be critical in capturing this opportunity.

How challenging do you find workforce recruitment and development?

The competition for talent is still very intense, particularly for areas such as digital, advanced analytics, and automation. The improved reputation of global pharma companies through the pandemic will, however, have improved access to some talent.

Elizabeth Topp, Chief Scientific Officer, NIBRT

KEY THOUGHTS

"I expect that we'll see broader application of vaccines in the future, not only for preventing disease but also for disease treatment, such as cancer."

"There will be an upsurge in RNA-based therapies, while cell therapies will see slower introduction."

"Priorities for biopharma manufacturing innovation should include the development of continuous manufacturing with closed loop process control, supported by inline monitoring of product quality."

What are the most exciting advances in terms of vaccine technologies and manufacturing processes?

Certainly the most exciting advance in the last two years has been the rapid development, approval, and distribution of mRNA- and DNA-

based vaccines for COVID-19. This is precedent setting and will likely enable more rapid development and approval of future drug therapies in this class.

Post-pandemic, how do you think activity around vaccines will change? Will it drop back to normal levels, or will vaccines still be a key focus point?

I expect that the focus on vaccines will continue to be greater than in pre-pandemic times. Previously, vaccines were often viewed as niche areas in the pharmaceutical industry, eclipsed by drugs for life-threatening or chronic diseases, like cancer and diabetes. Vaccines took center-stage during the pandemic, and I expect that we'll see broader application of vaccines in the future, not only for preventing disease but also for disease treatment, such as cancer.

What types of biopharmaceutical products do you think will be the most important in the coming 5–10 years?

I don't have a crystal ball, but here's my best guess: mAbs and



“I expect that we’ll see broader application of vaccines in the future, not only for preventing disease but also for disease treatment, such as cancer.”

recombinant proteins will continue to dominate. But there will be an upsurge in RNA-based therapies, while cell therapies will see slower introduction – perhaps accelerated by a shift to allogeneic technologies.

What are the biggest challenges when it comes to bringing new products to market?

Time!

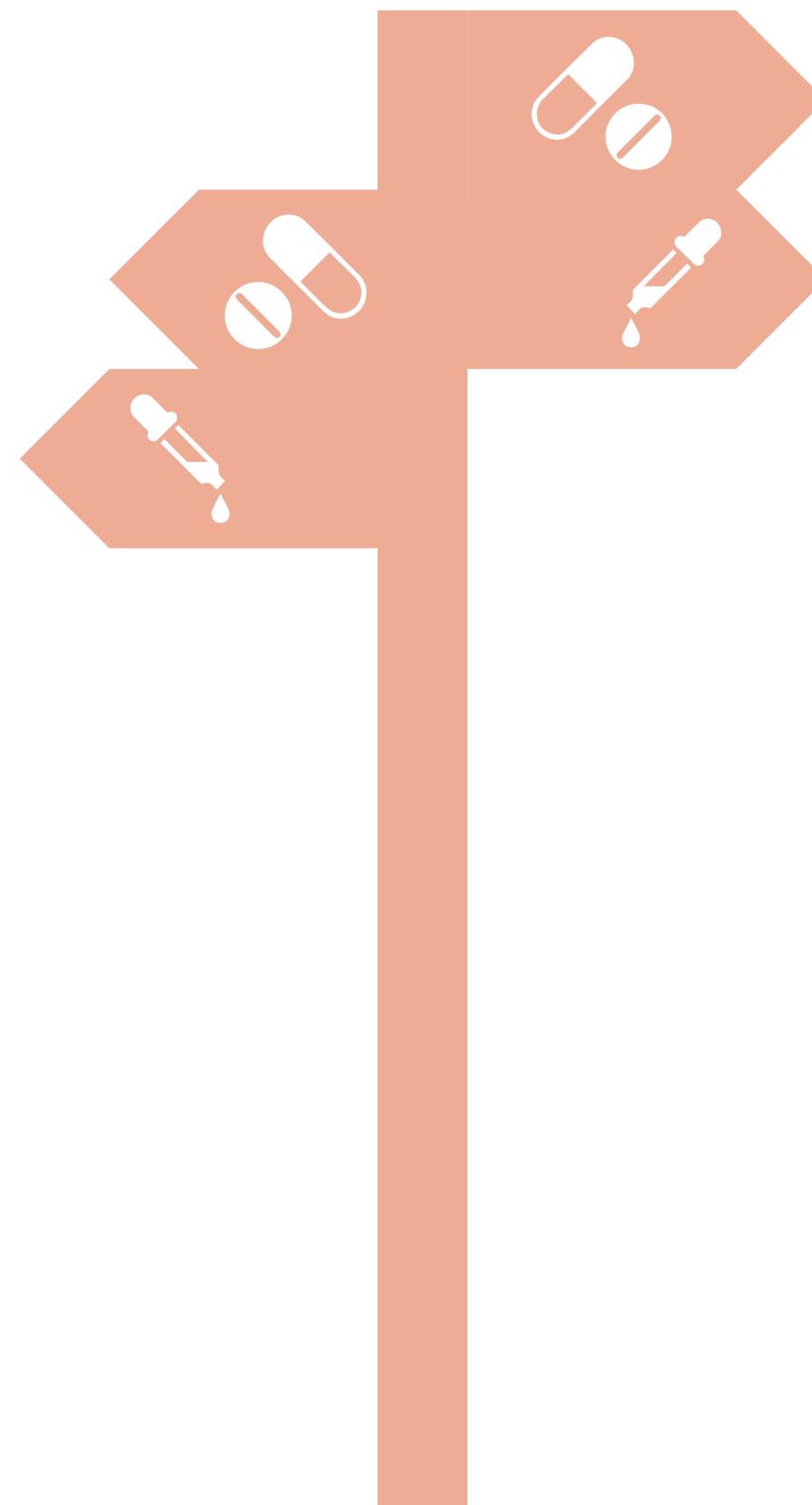
What areas of biopharma manufacturing should be a priority for future innovation and why?

Right now, we’re making highly advanced medicines, but not with advanced manufacturing. Compared with the rest of the chemical process industry, pharmaceuticals are low-volume, high value-added products that are highly regulated. As a result, pharmaceutical manufacturing has long relied on relatively low-tech manufacturing methods, such as batch processing, open loop process control, and unit operations with low efficiency. For example, lyophilization

(freeze-drying) is used to manufacture about 40 percent of marketed protein drug products and has less than 5 percent energy efficiency. Priorities for biopharma manufacturing innovation should include the development of continuous manufacturing with closed loop process control, supported by inline monitoring of product quality. These changes could improve process efficiency and throughput while maintaining – or even improving – the quality, safety, and efficacy of the finished products.

How challenging do you find workforce recruitment and development? And what best practices would you recommend to address this challenge?

Recruiting and retaining a talented workforce is becoming a challenge for us here at NIBRT, and for the industry as a whole. “Bootcamp” training programs to rapidly upskill workers who’d like to enter the biopharmaceutical industry are a possible solution. We’re working on that at NIBRT, too, but we can’t claim to have solved the problem even for ourselves.



Igor Splawski, Chief Scientific Officer, CureVac

KEY THOUGHTS

“The pandemic has shown that, by working together through partnerships and collaboration, development timelines for vaccines and other drugs could potentially be shortened.”

“For many of the vaccine companies, their standing and attention within the industry has been elevated and is now enabling them to act from a much stronger position.”

“The industry is highly competitive across the globe, so attracting and retaining an efficient and qualified workforce is a challenge.”

What changes have been ushered in by the COVID-19 pandemic in the biopharma industry overall?

The COVID-19 pandemic has triggered changes for the biopharma industry that will be felt for many years to come. In particular, the unprecedented acceleration in the timescale from the initiation of clinical trials to the regulatory approval and mainstream production of the first mRNA vaccines highlighted the importance of this sector to global health.

Although the vaccines were developed extremely quickly, there were no compromises on safety, which has always been the highest priority. The pandemic has also shown that by working together through partnerships and collaboration, development timelines for other drugs and vaccines could potentially be shortened. This will involve both engagement and consultation across regulators and suppliers, and the continuing deployment of innovative digital and analytical technologies that have emerged in recent years and thrived during the pandemic.

What are the most exciting advances in terms of vaccine technologies and manufacturing processes?

As we are still only beginning to explore the power of mRNA technology. The accelerated application of this technology to SARS-CoV-2, without compromises on safety, has been astonishing. The global need for a vaccine provided the impetus to transfer scientific expertise so that candidate mRNA vaccines could enter development quickly. With this validation as a basis, mRNA offers a great potential that goes beyond COVID-19.

At CureVac, we have focused our mRNA-based pipeline on three therapeutic areas: prophylactic vaccines, cancer immunotherapies, and molecular therapies. In tandem with the development of our first COVID-19 vaccine, we ramped up manufacturing processes to



“For many of the vaccine companies, their standing and attention within the industry has been elevated and is now enabling them to act from a much stronger position.”

ensure the clinical supply of vaccines. Meanwhile, we also put in place the logistics and supply chains necessary to increase production and meet commercial demand. This period of creativity also propelled the development of alternative manufacturing methods. And that’s how we accelerated the development of a mobile rapid response unit that could be used to contain local outbreaks.

Post-pandemic, how do you think activity around vaccines will change? Will it drop back to normal levels or will vaccines still be a key focus point?

The fight against COVID-19 is continuing and this pandemic has highlighted the impact a global outbreak can have on all aspects of everyday life. The existing successful COVID-19 vaccines have shown just how effective a vaccination technology can be. Moreover, it is crucial to build on these experiences. For many of the vaccine companies, their standing and attention within the industry has been elevated and is now enabling them to act from a much stronger position.

What types of biopharmaceutical products do you think will be the most important in the coming 5–10 years?

Scientific advances are being made continuously. However, these technologies often need time to mature before gaining acceptance

and implementation. For CureVac, it has been a 20-year journey with mRNA so far, but this is not unusual. Other technologies such as RNAi and gene therapy have needed a similar period of time to mature.

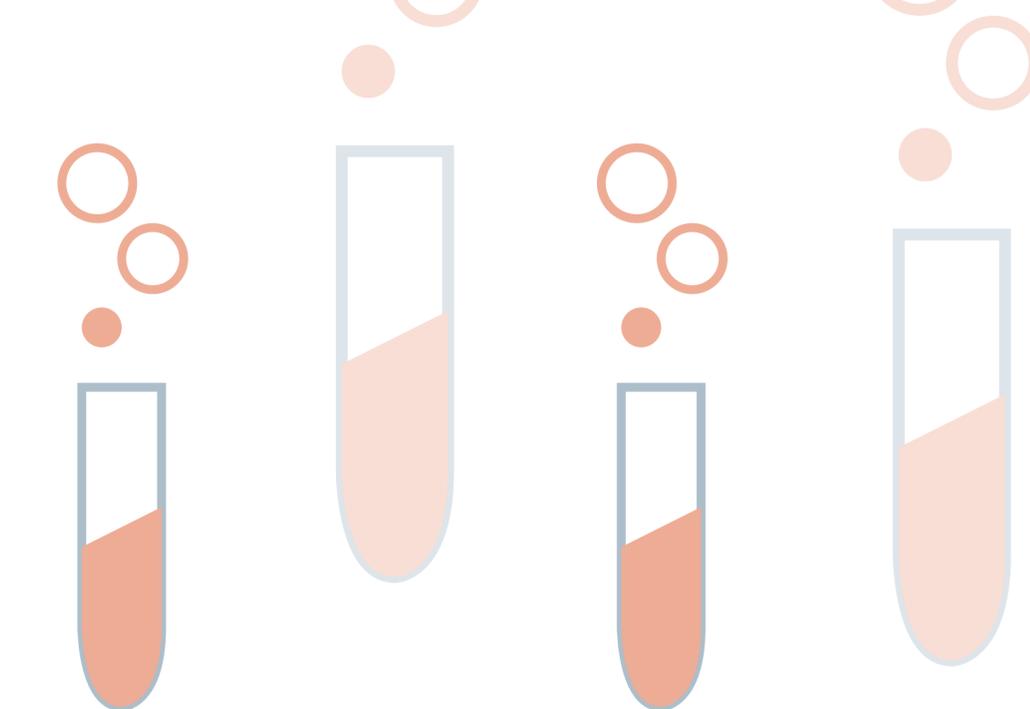
Over the next 5–10 years, we expect to see several technologies hit maturity, of which mRNA will be one. We expect it to pass through modifications and evolution to create the next generation of products. We are seeing this in the application of mRNA technology to the treatment of cancer, as well as rare diseases.

What areas of biopharma manufacturing should be a priority for future innovation and why?

Biopharmaceuticals are large and complex molecules. Despite many advances over the years, biopharma manufacturing still involves many separate, moving processes. In the future, we expect companies to prioritize improvements in product quality, which would expand capacity, increase the speed to market, and lower manufacturing costs.

What are the biggest challenges (for pessimists) or biggest opportunities (for optimists) when it comes to the growth of the biopharma industry?

The COVID-19 pandemic has shown where the challenges and



the opportunities lie for RNA companies. The new forms of collaboration in the value chain and in new processes for the approval of new vaccines enabled the development of safe vaccines to start combating the virus within a very short time. We have seen that the industry is able to become a problem solver. We’ve also seen what can be achieved when companies provide infrastructure and implementation power, thus also providing leverage that can help innovative biotech companies bring medical innovations to market.

How challenging do you find workforce recruitment and development? And what best practices would you recommend to address this challenge?

The industry is highly competitive across the globe, so attracting and retaining an efficient and qualified workforce is a challenge. That said, we have found that the main reason why people want to work in this industry is the belief that they can make a real difference. We are also increasingly bringing in people from elsewhere in pharma who can contribute expertise at the backend of the value creation process, in the area of commercialization. I also think it is important to always create a free space for employees to exchange ideas so that a company’s culture can continue to grow.

Catarina Flyborg, Vice President, Cell & Gene Therapy, Cytiva

KEY THOUGHTS

"I think the most important thing is the need to construct the capacity for rapid scale up. This is what drives the need for flexible manufacturing sites."

"mRNA isn't new. There has been research around this for more than 20 years, but now there has been a breakthrough."

"For any company, it's very important to bear in mind that the requirements of students today are very different from those of previous generations. We must listen, understand, and be agile in meeting the needs and the wants of those individuals."

What changes have been ushered in by the COVID-19 pandemic in the biopharma industry overall?

We were forced to build out capabilities across all activities that relate to healthcare. The greatest challenge was getting hold of talent in life sciences, in IT, and across all aspects of healthcare. I have heard the same thing whenever I have spoken to people working in academic institutions, and any other collaborator: talent, talent, talent. This is what we have been coming back to all the time.

There is a major need for courses, development, and education to address the gap in talent we are facing. Given the ongoing pandemic, Cytiva and others have developed virtual courses to address the needs of the industry. Managing this required considerable innovation, but we did it.

What types of biopharmaceutical products do you think will be the most important in the coming 5–10 years?

I think monoclonal biologics will continue to see a very nice growth trajectory, and the double digit growth and massive volume we are seeing today will help these biologics to hold on to their dominant position.

Having said that, cell and gene therapies have even higher growth rates. If we project that some ten years into the future, then they will hopefully attain the same level as monoclonals.

Then, of course, there is mRNA. It is seeing enormous attention right now, and there is serious promise regarding the research thus far. I think its interest has spread partly by word of mouth. Just two years ago, I would say mRNA was only well known by a small number of people – mostly researchers trained in life sciences or biochemistry. Nobody else knew about it. But now, everybody is talking about mRNA!





What areas of biopharma manufacturing should be a priority for future innovation and why?

I believe there is enormous potential for advances triggered by cell and gene therapy. The reason I say that is because this field is transforming the conversations into how to cure disease – not just treat and take away the symptoms.

Aside from that, I think the next most important development will be in the digital space – after all, that’s really where we can make a big difference regardless of the therapy being manufactured. The digital sphere – automation and artificial intelligence – will be a game changer.

What are the biggest challenges (for pessimists) or biggest opportunities (for optimists) when it comes to the growth of the biopharma industry?

Returning to the point I started with, I think the challenge will be to attract talented people into the life sciences; to outcompete the big technology companies of the world and get the best and the brightest into our industry, ready to put their brain power to work. I absolutely think this will be the biggest challenge.

How challenging do you find workforce recruitment and development? And what best practices would you recommend to address this challenge?

As you can tell from my previous answers, this is a question that we work with every day.

For any company, it’s very important to bear in mind that the requirements of students today are very different from those of previous generations. We must listen, understand, and be agile in meeting the needs and the wants of those individuals. Think about it: 2022 is nothing like 2012.

We need to understand what drives people today, we need to understand how those drivers have changed, and we need to accept that as a consequence we must change. The industry has begun to do this, but if you take a look at the structure of the companies, you will see that more work is needed.

What are the most exciting advances in terms of vaccine technologies and manufacturing processes?

I’ve been around for long enough to see the rise of the life sciences business. The most exciting development right now is not that biologics per se are on the rise, but the fact that during the past 24 months we have seen the development of mRNA.

mRNA isn’t new. There has been research around this for more than 20 years, but now there has been a breakthrough. We can now use specific mRNA treatments as vaccines, and I think that is by far the

most exciting thing going on in the field. It is also exciting to see that we can use mRNA not only for vaccines, but also as therapies for various types of precision medicine.

I think the other big reason to be excited is the rollout of digital automation. This development may not be of the same magnitude as mRNA but, going forward, greater predictive analytics could be a game changer.

Post-pandemic, how do you think activity around vaccines will change? Will it drop back to normal levels or will vaccines still be a key focus point?

I think that is the billion dollar question!

Whatever the case turns out to be, I think the most important thing is the need to construct the capacity for rapid scale up – and that drives the need for flexible manufacturing sites. The Omicron variant showed us the importance of this; in such cases, we simply do not know what we will need next month. Flexibility can help solve the problem.

The second kind of change we may see is that vaccines or the technology around vaccines can also be used for therapeutics. So the knowledge and the skill sets and the understanding we gain now can also be used not only in preparation for trouble, but also for future medicines and cures.

Rick Bright, CEO, Pandemic Prevention Institute, Senior Vice President of Pandemic Prevention and Response, The Rockefeller Foundation

KEY THOUGHTS

"We have been given a chance to change the narrative, build upon these lessons learned, and work collaboratively towards a more equitable world to improve the health and safety of everyone. It is our moment to leverage or squander this opportunity to change."

"If you don't dream big and set big goals, you will only ever achieve a next iteration and your competition will then change the field. You'll be left holding your Betamax tape in a digital world."

"We need a host of new technologies. Not every technology will work for every threat in the future. It is important that we strengthen both the technologies of today while we work to improve and integrate the technologies of the future."

What changes have been ushered in by the COVID-19 pandemic in the biopharma industry overall?

COVID-19 made long-term priorities immediate imperatives. There has been a rapid uptake of digital technologies by the biopharma sector across everything from clinical trials to data collection and sharing to

the incorporation of genomic sequencing into clinical health settings. The ability to use digital technology to support clinical trials – allowing more virtual monitoring, data collection and evaluation – is an advance that can democratize research and data. Representative data, whether in an R&D context or for pathogen surveillance, is essential. COVID-19 has shown again and again the human and economic cost of gaps in global tracking—where capabilities for genomic sequencing and sharing of these and related data are missing. The Sars-CoV-2 virus evolves and gets ahead of us when we are not looking. We've also seen a rapid expansion of simpler technologies for genomic sequencing and the sharing of those data rapidly among scientists into international platforms such as the GISAID community database. It's going to be crucial to ensure the momentum around digitalization that supports the collection, use, and action on representative data continues as the pandemic wanes and eventually ends.

What are the most exciting advances in terms of vaccine technologies and manufacturing processes?

R&D efforts to develop COVID-19 vaccines have been among history's greatest scientific achievements. In its first phase, countries, companies, and labs funded a number of vaccine technologies in the hope that some would result in safe and effective vaccines for a global vaccination campaign. In 2021 Johnson & Johnson/Janssen, Pfizer-BioNTech, and Moderna projected an ability to deliver over four billion doses – and then over seven billion doses in 2022.

Everyone was surprised with how well mRNA vaccines performed, but we shouldn't think it will solve all of our vaccine needs. It is important to sustain a variety of vaccine platforms to ensure we have supply and flexibility to respond to a variety of pathogens.

It's also important to accelerate the development of new approaches to manufacturing for other vaccines. Even before COVID-19, my colleagues and I were focused on finding alternatives to egg-based production for influenza vaccines, like Flucelvax, which is produced in mammalian cells and Flublok, which uses recombinant technology.



Both of these cell-based approaches may provide a speed advantage and be a closer match to circulating human influenza viruses than vaccines produced in eggs.

Accelerating vaccine production requires collaboration – and it's been exciting to see this happen among firms that would normally be competitors. For example, Merck is manufacturing vaccines for Johnson & Johnson. London-based GSK and Novartis in Switzerland are manufacturing doses for CureVac, based in Germany. For the vaccine it developed with the University of Oxford, AstraZeneca arranged collaborations with multiple manufacturing facilities across more than a dozen countries, including the Serum Institute of India, to produce more than 3 billion vaccine doses.

Producing vaccines can be more complex than producing small molecule drugs; so truly scaling production to the required levels will require technology and knowledge transfer to support a global sustained workforce, skilled in vaccine production. This must include sustained investments in and support for regional production platforms in Central and South America, Asia, and Africa. Moving to regional, national, and local production capacity and capability is absolutely essential for long-term, sustainable, and equitable efforts to contain outbreaks and prevent future pandemics.

Post-pandemic, how do you think activity around vaccines will change? Will it drop back to normal levels or will vaccines still be a key focus point?

Prior to COVID-19, only a few companies produced vaccines. Now everything about vaccine R&D has been above the fold for months.

This is not the first pandemic and it will also not be our last. Through the work to accelerate COVID-19 vaccines, industry has invested

heavily in both manufacturing of vaccines, and scale up of supplies and technologies needed for vaccine production. It is imperative that we work collaboratively to ensure that advances made are sustained, used in non-emergency times, and are ready to surge again when needed. If we allow facilities to sit idle until the next emergency, we will be back at square one with outdated equipment, outdated processes, outdated quality systems, and lack of a trained workforce to spring into response mode.

If past experience remains the norm, the world will forget this pain, funds will dry up, and capabilities will rapidly diminish. We have been given a chance to change the narrative, build upon these lessons learned, and work collaboratively towards a more equitable world to improve the health and safety of everyone. It is our moment to leverage or squander this opportunity to change. We know the consequences if we don't.

What types of biopharmaceutical products do you think will be the most important in the coming 5–10 years?

We need a host of new technologies. Not every technology will work for every threat in the future. It is important that we strengthen both the technologies of today while we work to improve and integrate the technologies of the future. When SARS-CoV2 was identified, it was the ability to prioritize more advanced or proven technologies for rapid scale-up to meet the timeline and demand. Little risk was taken and therefore, limited support went to technologies that might be better than the ones prioritized. We need to continue innovating in the biopharmaceutical space. We need to improve processes to reduce the time and footprint of production to drive it into more regional and local operational sites for improved access around the world.

We also need to improve formulation of medicines to simplify delivery and administration of drugs and vaccines. For a global response, we need

to innovate out the needle and syringe, moving to oral and transdermal administration. Cold-chain requirements on medicines limit access in many of the hardest to reach communities. We have come through a period that has shown us the art of possibility with innovation and collaboration. I know that there are many innovations and entrepreneurs who are hard at work to take today's best technologies and completely transform them into a future world where medicine can reach more people, sooner, at a lower cost, and without many of the barriers that are currently slowing the global response to SARS-CoV-2.

I also believe that data will be a new form of medicine. By connecting and sharing more disparate data types, both personal and environmental, we will generate more in-depth knowledge of what is happening around us and how we respond to various pathogens and diseases. We can generate a much earlier global warning system to alert us when a new threat has emerged in humans, and we can respond more rapidly to stop it before it becomes a global crisis. By identifying and harnessing knowledge around biomarkers, we can detect and stop cancer sooner, detect and treat sepsis sooner, and more appropriately detect and bend the curve on antimicrobial resistance. We are surrounded by data, but it is fragmented, siloed, and buried under layers of barriers that are preventing it from being democratized and leveraged to improve human health and save lives.

I see a change on the horizon; a world where we are all more willing to participate and share more information for the greater global good.

What are the biggest challenges when it comes to bringing new products to market?

Sometimes, the most challenging part of having a new product is simply getting it into the marketplace. There are often market force headwinds that crowd out the introduction of new products, even

when they are improvements over the status quo. For new tests that can diagnose sepsis in just a few hours, it is extremely challenging to replace traditional culture tests that take days to detect a bacterial infection and even longer to determine the correct antibiotic regimen. Millions of people die each year because sepsis is not detected early and they are often given generic antibiotics that may not be effective against their infection. I, personally, experienced this a few years ago when I nearly had to have my thumb removed from a simple garden nick that led to a MRSA infection. After experimenting with seven antibiotics and an antifungal, doctors finally received results from a culture assay. Once we learned the appropriate antibiotic, the insurance company immediately sent a letter informing me it would not be covered.

The second huge challenge for new products, such as novel antibiotics, that are critically needed to address the tsunami of antibiotic resistant bacteria among us, is that insurance and CMS often don't pay for these new drugs. If they do, reimbursement is often limited to what a generic (ineffective) drug might cost. There is no market incentive for companies to develop new diagnostics or antibiotics. Reimbursement is not value-based, taking into consideration the US\$1 billion or more development costs, the actual healthcare costs that will be saved by earlier and more effective treatment, and not even the number of lives that would be saved. We have amazing new medicines and devices that have been developed and are sitting in a warehouse instead of in hospitals, formularies, or homes where they can be saving the lives they were developed to reach. We must find a way to address these challenges, urgently.

What areas of biopharma manufacturing should be a priority for future innovation and why?

We must incorporate new production technologies that are more efficient, less toxic, and have a smaller footprint, so they can be regionalized (or even localized) to improve access while reducing cost.

Great progress has been made in continuous manufacturing for small molecule drugs. Many production steps are streamlined to reduce waste and human error while improving production efficiency and yield. I was leading this work, in collaboration with the FDA, while I was the Director of BARDA. The benefits are huge, and this is now being adopted by several manufacturers. We also supported work to reduce the footprint of the production space. In fact, we are driving production for some drugs down to a space the size of a small kiosk. Imagine being able to walk up to a kiosk, enter your prescription and have your medicine produced on demand; imagine that capability in every hospital or corner drug store. It would have a huge impact on access and supply chain challenges.

Now look at vaccines. We are making great progress in the broad field of vaccines that can be synthesized (like mRNA). I have seen technologies the size of a home printer that can print mRNA onto a patch. It is not farfetched to imagine we will progress to an ability to print our own vaccines on a patch in our homes and self-apply. No more needles or cold chain challenges. Imagine what that could do for access to vaccines, especially when a surge is needed for a broad response. There are many ways to get there, but I think technology priorities should focus on improved efficiency, regional production, and removal of distribution and administration barriers that are hampering global access to lifesaving medicines.

What are the biggest challenges (for pessimists) or biggest opportunities (for optimists) when it comes to the growth of the biopharma industry?

To feed into the pessimist's mind, I think they will still allow yesterday's barriers, either technical or regulatory, to constrain their approach and goals. There are many convenient walls to see if a person only lives by navigating walls. But the pandemic has shown

us that all walls can be moved and all obstacles can be surmounted. This is where opportunity lies for the optimist in realizing the power of collaboration on a global scale and the ability to converge novel disciplines to see challenges through a new perspective... and knowing that there is always a way forward. If you don't dream big and set big goals, you will only ever achieve the next iteration and your competition will then change the field. You'll be left holding your Betamax tape in a digital world.

How challenging do you find workforce recruitment and development? And what best practices would you recommend to address this challenge?

As I have always said, our team is our secret sauce. I have always been mission-focused and if you have a compelling mission, it is easier to recruit the right people who are just as passionate about the mission. Passion is as important as technical skill and team passion is an addictive synergy when it comes together. I am in a fortunate position now of creating and launching a completely new federated approach, incubated within The Rockefeller Foundation, to detect threats and provide an early warning signal to the world and prevent another pandemic. To be successful, it's important to think outside the box and to recruit outside the traditional field of public health. If current public health approaches were effective, we would not have experienced 2020-2022 the way we have. I am recruiting from fields of finance, physics, quantitative analysis, crypto, and decentralized or distributed systems. My goal isn't to replace traditional public health systems, but instead to bring 21st century tools and analytics to a system that hasn't changed much over the centuries. As much as it is modern and technologically advanced, the future is based on foundational principles of collaboration, sharing, equity and trust – critical things that we didn't have in place before the pandemic hit. This is a mission that is not difficult to recruit for, especially after the devastation we have seen.

Charles Morris, Chief Medical Officer, Celyad Oncology

KEY THOUGHTS

"Vaccines have always had a unique niche in the therapeutics space, and I think they will retain their important place in the biotech ecosystem."

"If we look at oncology, in particular, we've seen some interesting shifts over the last two decades that will most likely continue in the coming years."

"Expanding the use of new therapies typically proves to be a major challenge, sometimes minimizing the full potential of a novel treatment or modality."

What are the most exciting advances in terms of technologies and manufacturing processes?

The transition from autologous to allogeneic manufacturing processes is the biggest and most exciting advancement in CAR T right now. The idea that we can build processes that will allow us to serve multiple patients at once from a single manufacturing run using a single healthy donor is very exciting and really has been embraced by the CAR T field. These advances will allow us to begin with higher quality material and less variance in the overall quality of therapy.

We're now figuring out how to scale up towards a process that is sufficient for a later stage registrational trial and commercial stage. This means larger quantities of cell therapy but still maintaining the high levels of quality and consistency needed for an effective treatment.

Post-pandemic, how do you think activity around vaccines will change? Will it drop back to normal levels or will vaccines still be a key focus point?

Vaccines have always had a unique niche in the therapeutics space, and I think they will retain their important place in the biotech ecosystem. We're keeping an eye on where else vaccine technologies can be taken to benefit other spaces – are these new technologies or modalities complementary to what we're doing in CAR T? How else can they be implemented to advance therapies being developed outside the vaccine space?

What types of biopharmaceutical products do you think will be the most important in the coming 5–10 years?

If we look at oncology, in particular, we've seen some interesting shifts over the last two decades that will most likely continue in the coming years. When I first started my career in the sciences and oncology, I was working within small molecules, and it's been incredible to see the number of modalities that now exist to try and tackle these diseases, such as CAR T.



“Expanding the use of new therapies typically proves to be a major challenge, sometimes minimizing the full potential of a novel treatment or modality.”

In terms of other oncologic therapies, there are bispecific antibodies, antibody-drug conjugates, and a number of immunotherapeutics that use the nuances of the immune system against these multifaceted tumors. In addition, protein degradation is yet another exciting field that holds promise.

I couldn't be prouder to be a part of the work that the oncology community is doing, and I look forward to seeing the field continue to evolve in the coming years.

What are the biggest challenges when it comes to bringing new products to market?

Bringing a new product to market is always a major endeavor that involves a sizable team with different backgrounds including business, science, law, and so on. In the case of allogeneic CAR T, the challenge is scalability. How do we make CAR Ts like other biologics, or make them more like a small molecule drug that can truly come “off the shelf”? Figuring out how to take what we're doing now and make it translatable to the physician's office further down the line will also be a challenge. A therapy has to be relatively straightforward to administer if we are to succeed at making this a viable option that is adopted as a part of the oncology armamentarium.

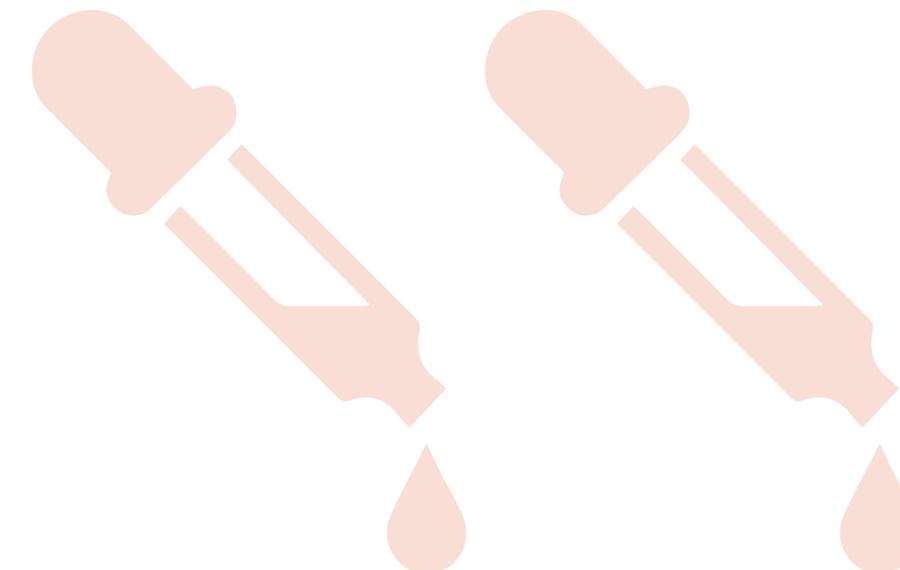
What areas of biopharma manufacturing should be a priority for future innovation and why?

The goal for manufacturing is always to streamline the process while maintaining the quality of the product and remaining cost-effective. New products are being developed all the time, and thus processes continue to evolve.

What are the biggest challenges (for pessimists) or biggest opportunities (for optimists) when it comes to the growth of the biopharma industry?

Critical to the oncology space – and ultimately relevant to the biopharma industry as a whole – is the concept of taking an approved therapy and expanding its use, primarily by moving it further upstream in the recommended treatment paradigm for a disease. And that means bringing therapies to new patients by making them first-or-early-line treatment options used for the largest portion of a particular patient population.

Most drug developers start by identifying a patient population where there's great need but also the maximal chance for clinical benefit.



These are often small target populations who provide evidence that a new treatment strategy works. After the benefit is shown, the biggest challenge is proving that a potentially beneficial treatment can help a larger group of patients. Generally, you have to determine whether there are complementary therapeutics already approved that could work in conjunction with your investigational agent to make it more effective in larger addressable populations or perhaps allow for you to expand the pharmaco-economic benefit of a therapy. Expanding the use of new therapies typically proves a major challenge, sometimes minimizing the full potential of a novel treatment or modality.

How challenging do you find workforce recruitment and development? And what best practices would you recommend to address this challenge?

Workforce recruitment and development has been fantastic, particularly in Belgium. We've recruited individuals able to help us with anything from research and clinical development to manufacturing. That said, there are always hurdles in keeping individuals engaged, motivated, and connected to the company culture, especially during the pandemic. Making sure the executives connect with the wider team is especially important.

Fabian Gerlinghaus, Co-Founder and CEO Cellares

KEY THOUGHTS

“The sudden increase in demand for viral vectors to test and manufacture vaccines was something of a sneak preview of the demand to come from cell and gene therapy manufacturers in the years ahead.”

“The brass ring that the industry is reaching for is true personalized medicine. To get to a place where precision treatments like cell therapies can be the standard of care, we need scalable, innovative solutions to decentralize and automate GMP manufacturing.”

“We’ll reach a point where manufacturing capacity will equal market demand for personalized therapies in specific indications”

What changes have been ushered in by COVID-19 pandemic in the biopharma industry overall?

COVID-19 was a wake-up call for the industry in so many ways and across so many areas, including supply chain fragility, manufacturing capacity limitations, and staffing constraints. Many of these strains

already existed, but the pandemic exacerbated the issues. It has motivated the industry to explore new solutions in a more robust manner, with a new emphasis on business continuity planning to avoid or minimize future disruptions.

For cell therapies in particular – where manufacturing is a logistical challenge and meeting patient demand is daunting – the pandemic accentuated the need for more automated processes. These will unlock the potential of skilled labor by automating established processes so scientists can focus their attention on innovating new processes. Automation will also relieve some of the challenges around retaining and developing workers, allowing employees more flexibility and remote options given the improved predictability and control.

Supply chain disruptions have encouraged innovation to find more disruption-resilient manufacturing approaches. In areas like autologous cell therapies, in which cells are extracted from patients at the hospital, transported to distant manufacturing facilities and then returned to the hospital, innovation could facilitate decentralized manufacturing located closer to the point of care. One significant benefit of this model is decreased turn around time (TAT) allowing the patient to receive the cell therapy a few days sooner.





Significantly, the general public has developed a deeper appreciation for our industry, thanks to the important work we are doing in response to the COVID-19 pandemic.

What are the most exciting advances in terms of vaccine technologies and manufacturing processes?

We were all astonished by the speed of companies like Moderna, who had a vaccine candidate in vials for clinical testing just six weeks after getting access to the SARS-CoV-2 genome. Automation then played a big role in scaling up manufacturing and getting COVID-19 vaccines to patients quickly.

I would like to see that mindset become more widespread in biopharma. In practical terms, this will require standardization across supply chains and manufacturing. Most companies believe their processes give them a competitive advantage in the marketplace. However, standardization can be a rising tide for all boats, while still leaving space for new technologies to innovate.

Advances in vaccine technology will have longer-lasting benefits as well. The sudden increase in demand for viral vectors to test and manufacture vaccines was something of a sneak preview of the demand to come from cell and gene therapy manufacturers in the years ahead. That need is spurring additional manufacturing capacity, as well as development of new viral vectors and engineered nanoparticles as delivery vehicles, which may help avoid similar supply chain stresses for cell and gene therapy as the market explodes over the coming decade.

Post-pandemic, how do you think activity around vaccines will change? Will it drop back to normal levels or will vaccines still be a key focus point?

Because much of the world still is not fully vaccinated against COVID-19, it's likely that we'll continue to see new variants, and it appears at least some people may require additional vaccines/boosters long-term. As the pandemic likely will develop into an endemic, we won't maintain the growth rates seen over the past two years, but activity will not return to pre-pandemic levels for the foreseeable future.

What types of biopharmaceutical products do you think will be the most important in the coming 5–10 years?

Cell therapies are approaching a critical inflection point. Over a thousand cell therapy clinical trials are ongoing, and the FDA expects 10–20 approvals for cell and gene therapy products every single year starting in 2025. Today, only autologous cell therapies are commercialized. These are made to order, one dose at a time, using the patient's cells as the starting material. End-to-end high-throughput manufacturing automation solutions are showing that automation can drastically improve manufacturing and scalability.

The excitement around these therapies is warranted, as they have the potential to be curative for fatal illnesses with a single dose. The process is the product, meaning that as we solve the challenges of scaling up these therapies and get them to patients faster, the

benefits are likely to extend beyond just increased access. For example, decentralized manufacturing may allow for the use of fresh cell therapies without need for cryopreservation, and automation efficiency could improve output quality.

What are the biggest challenges when it comes to bringing new products to market?

Drugmakers often struggle with new therapies as they approach clinical trials, especially for novel modalities, because the processes needed to scale up manufacturing may not exist. Making enough of a product for commercial-scale manufacturing is a much bigger challenge compared with making enough doses for clinical trials.

Right now, cell therapies exemplify this issue. Although several products (each with unique manufacturing processes) have made it to market, demand continues to outpace supply. Manual manufacturing with high levels of personalization means longer vein-to-vein times and limited manufacturing capacity, which restricts the number of patients who can benefit from them. Addressing these bottlenecks with automation will go a long way toward accelerating access to this next generation of therapies for patients.

Cell therapies face other hurdles to commercialization too. Demonstrating potency, consistency, and traceability as these therapies scale to multiple countries and manufacturing sites can be difficult, due to unclear mechanisms of action and the complexities of assays needed



to properly characterize the product. Scaling quality control and release testing for autologous cell therapies faces another bottleneck, which can be resolved by automated next-generation technologies.

What areas of biopharma manufacturing should be a priority for future innovation and why?

The brass ring that the industry is reaching for is true personalized medicine. To get to a place where precision treatments like cell therapies can be the standard of care, we need scalable, innovative solutions to decentralize and automate GMP manufacturing. We need this not only to get today's clinical candidates over the finish line, but also to broaden access to innovative small companies and academics who can't afford to build facilities like a conventional GMP clean room.

Industry standardization across platforms and analytics should be prioritized to continue improving processes and help satisfy regulators on questions of product quality and consistency. We'll also need to see an emphasis on new sources of starting materials, with viral vector and other shortages during the pandemic underscoring the importance of flexibility in the supply chain.

The pandemic also accelerated the movement away from specialized treatment centers and toward point of care and home care. Just as automation and decentralized manufacturing enable better, faster

treatment of people wherever they are, innovative pricing models and advances in home and outpatient care will shape the future needs of cell and gene therapy manufacturing.

What are the biggest challenges (for pessimists) or biggest opportunities (for optimists) when it comes to the growth of the biopharma industry?

I see many reasons for optimism about industry growth. Recently we've seen heavy investment around COVID-19 and beyond. In cell and gene therapy, for example, we've seen investors setting records over the last year, despite slowdowns elsewhere. Public funders continue to support early research, and investors back novel ideas in a big way, particularly in the US.

And that's why we are undaunted by manufacturing hurdles in this space. The biopharmaceutical industry has a strong track record for overcoming obstacles like these, and we're on track to do so. Cell and gene therapies are at a tipping point relative to other innovations in a similar phase, where the technology is becoming available to make commercial-scale manufacturing feasible in a way that will lower the cost of care. By automating many manual processes, we'll streamline the entire GMP workflow from interoperable equipment to documentation, freeing up highly trained scientists to refocus on other high-value areas like asset

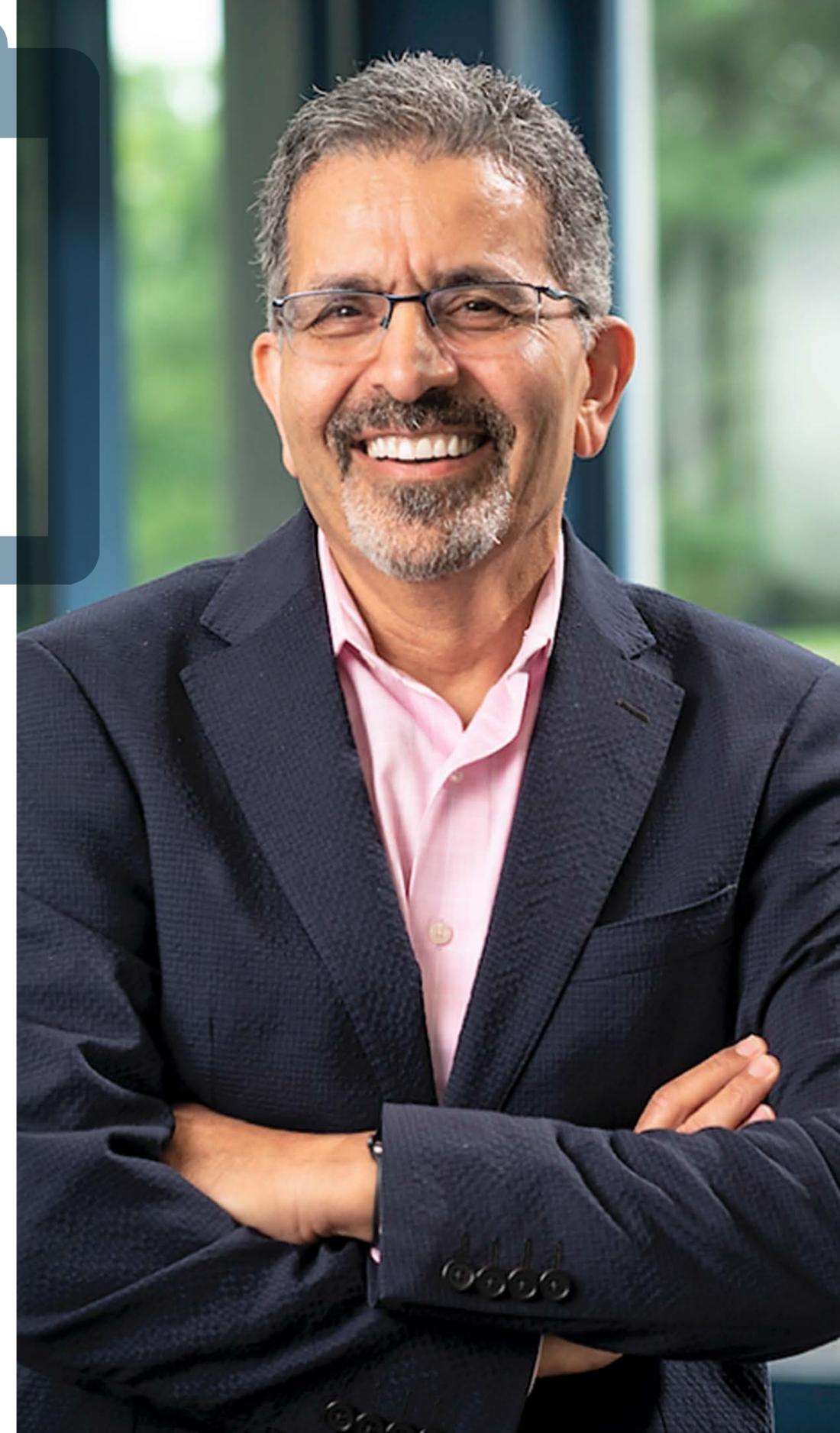
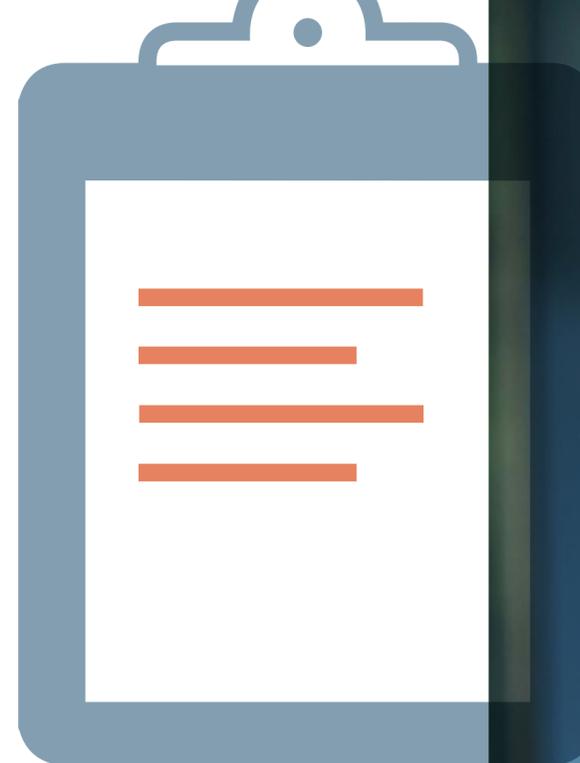
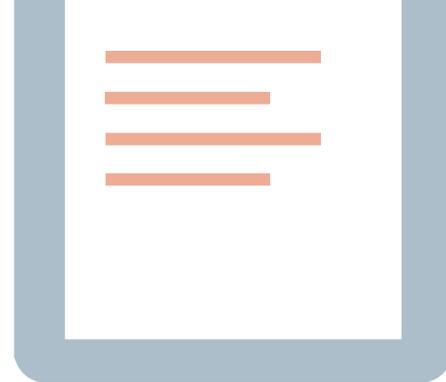
development, which will lead to more and better therapies. As we surmount these hurdles, we'll reach a point where manufacturing capacity will equal market demand for personalized therapies in specific indications.

How challenging do you find workforce recruitment and development? And what best practices would you recommend to address this challenge?

Recruitment is always a challenge in rapidly growing spaces. The FDA expects to soon be approving dozens of cell and gene therapies every year. Today, manufacturing is still highly manual, requiring lots of hands in the cleanroom. These positions are extremely stressful, often involving 12-hour shifts without breaks while holding a patient's life in your hands. Some companies are experiencing 60 percent turnover within a year – a bad number that gets worse when you realize that the training period for these highly skilled positions is often more than six months long.

Automation will be necessary to both improve quality and lower the time and costs for manufacturing, all in order to allow scale-up in a meaningful way across sectors. Beyond this, it will ease the crunch for talent in a space where too few individuals have the experience needed by reducing staff training time and experience requirements, unlocking even greater possibilities for these employees and the companies.

Parviz Ayazi-Shamlou, Thomas Jefferson University



KEY THOUGHTS

“The future belongs to vaccine manufacturing platforms that are linearly scalable and based on recombinant DNA technology. Traditional egg-based, killed, or attenuated vaccine manufacturing platforms would not have been able to respond fast enough to the pandemic.”

“Reducing manufacturing costs, increasing access to therapies, and speeding up time-to-market for new therapies including cell and gene therapy and next generation vaccines are the biggest challenges.”

“In addition to the cost of therapy, the shortage in skilled workforce continues to be a concern.”

What changes have been ushered in by COVID-19 pandemic in the biopharma industry overall?

Bioprocessing has responded positively – and aggressively – to the COVID-19 pandemic. Biomanufacturing has contributed significantly to the global fight against COVID-19, and the manufacturing platforms used for the production of the two leading vaccines have confirmed that the future belongs to vaccine manufacturing platforms that are linearly scalable and based on recombinant DNA technology. Traditional egg-based, killed, or attenuated vaccine manufacturing platforms would not have been able to respond fast enough to the pandemic.

The Pfizer-BioNTech and Moderna mRNA vaccines also confirmed the safety and efficacy of the non-viral delivery



“In addition to the cost of therapy, the shortage in skilled workforce continues to be a concern.”

platform based on lipid nano-particles (LNP). mRNA and LNP platforms combined with other technologies, such as the CRISPR CAS9 platform, are creating innovative approaches to deal with traditional drug development and drug delivery challenges; for example, viral vector delivery systems used in cell and gene therapy. Many disease areas with unmet needs will benefit from these platforms, including cancers, non-malignant blood disorders (such as haemophilia A and B, and sickle cell disease), neurological diseases, inflammatory diseases, and many other life threatening diseases.

What types of biopharmaceutical products do you think will be the most important in the coming 5–10 years?

Cell and gene therapy and RNAi therapeutics – all of these will benefit from mRNA, LNP, and CRISPR-CAS9 platforms

What are the biggest challenges when it comes to bringing new products to market?

Reducing manufacturing costs, increasing access to therapies, and speeding up time-to-market for new therapies (including cell and gene therapy and next generation vaccines) are the biggest challenges, in my view.

What areas of biopharma manufacturing should be a priority for future innovation and why?

Lack of effective, efficient, and scalable manufacturing platforms continues to be a concern. We need to use bioprocessing science and engineering principles to address the key issues with appropriate solutions and technologies. We have done this already for protein replacement therapies, including monoclonal antibodies. Advances in cell culture and media development combined with development

in purification design and operations have led to major reduction in manufacturing costs, which ultimately benefits patients. Right now, the manufacture of cell and gene therapy is where monoclonal antibodies were around three decades ago. We can and should use the platforms for monoclonal antibodies as a template to speed up the development process for cell therapies, gene therapies, and advanced vaccines. I am optimistic that we will do this.

What are the biggest challenges (for pessimists) or biggest opportunities (for optimists) when it comes to the growth of the biopharma industry?

In addition to the cost of therapy, the shortage in skilled workforce continues to be a concern. Thomas Jefferson University has major initiatives in this regard. It is very important to offer a range of credential programs and industry professional courses that reflect what industry needs.

Natraj Ram, Vice President, Innovation, Bioproduction and Martin Hornshaw, Senior Director, Enterprise Science & Innovation Partnerships, Thermo Fisher Scientific

KEY THOUGHTS

"Biopharma is trending toward the right fit therapeutic modality to address the challenge inherent to a particular disease."

"Though we have been successful in delivering therapies, the next phase of innovation for the biotech industry will be focused on delivering therapies in a more efficient manner."

"Innovation is difficult. If there isn't a focus on it – meaning it has to compete with the day to day – then it will never be a priority."

What changes have been ushered in by the COVID-19 pandemic in the biopharma industry overall?

Natraj Ram: The most valuable change ushered in by the pandemic was how our industry collaborated in an unprecedented manner to deliver life-saving vaccines and drugs for patients – that commitment to collaboration and doing whatever it takes to meet patient and public health needs is here to stay. We have also been able to bring

a new modality to use on a massive scale, navigating regulatory and quality pathways, and assuring safety and efficacy – all while accelerating drug development. Finally, from a bioprocessing standpoint, we have taken supply chain challenges head on, finding creative ways to overcome them – again with the purpose of delivering vaccines to the world.

Martin Hornshaw: I would add that COVID-19 has reinvigorated interest in the ability to automate science and manufacturing. Concepts such as automated science are on the table for discussion. How do we develop laboratories that can operate without human intervention?

What are the most exciting advances in terms of vaccine technologies and manufacturing processes?

NR: Though the development of mRNA-based vaccines is an exciting advance that should pave the way for many more drugs, I consider the awareness that the pandemic has created on preventive healthcare, namely vaccines, as one of the most exciting advances – particularly as vaccines have historically been an under-appreciated and under-funded modality.

In terms of advances in manufacturing processes, the use of affinity-based purification of mRNA represents a significant advance, as it provides a platform, much like the Protein A affinity for mAbs, for accelerating discovery and development of mRNA-based vaccines and therapeutics.

MH: mRNA has proven itself as a modality that can move from viral sequence to the "public arm" in record time. This development continues apace, with second-generation mRNA vaccines already in development with the goal to reduce reactogenicity, improve stability, and so on. mRNA is moving from COVID-19 to other infectious diseases and a wider set of indications, and will move to therapeutic use more widely. This will be the third generation of mRNA.

There are also exciting manufacturing advances on the horizon for mAbs and emerging therapies. When it comes to mAbs, the focus is on driving efficiencies. For emerging modalities, such as cell therapy

Natraj Ram



Martin Hornshaw



and mRNA-based therapies, the most exciting advances will come in the form of workflow solutions. Manufacturing mRNA is quite different compared with the general bioprocess that produces a monoclonal or similar biotherapeutic. The raw materials are essentially enzymes, nucleotides and linearized plasmid DNA (pDNA) grown in bacteria. In vitro transcription from the pDNA generates the mRNA which is co-transcriptionally or enzymatically capped.

What types of biopharmaceutical products do you think will be the most important in the coming 5–10 years?

NR: In my opinion, all the different modalities will be equally important – each catering to the therapeutic application that it is the most effective in. I strongly believe that there is no one size fits all. Therefore, we should be continuing to pave the road ahead for each of them – driving costs down for antibody and vaccine products, and enabling advanced therapies, such as cell and gene therapies.

MH: Biopharma is trending toward the right fit therapeutic modality to address the challenge inherent to a particular disease. I don't see this changing. All modalities are relevant. Having said that, there is huge investment in advanced modalities; already for mRNA, we are looking beyond the basic unmodified mRNA vaccine to developing nucleoside-modified mRNA, circular RNA, and self-amplifying mRNA to make mRNA more durable in terms of its expression. Developments in lipid nanoparticles, exosomes, and other modalities for better delivery will also continue apace.

What are the biggest challenges when it comes to bringing new products to market?

NR: We have been very successful as an industry in bringing new products to market, as evidenced by our recent vaccine efforts. However, it is important that we continue to focus on making therapeutics available to patients faster and at lower cost, while maintaining the level of quality.

Vaccine development has provided us a jump start in building some approaches and mechanisms that will streamline the process, and we've also seen increased adoption of solutions, such as single-use technologies, which are creating additional manufacturing efficiencies and cost-savings benefits. Many emerging biotechs and established players are also choosing to leverage CDMOs, taking advantage of their agile and flexible supply chain offerings that can scale up or down to meet the diverse requirements of the industry so we can bring innovative medicines to patients faster.

What areas of biopharma manufacturing should be a priority for future innovation and why?

NR: Though we have been successful in delivering therapies, the next phase of innovation for the biotech industry will be focused on delivering therapies in a more efficient manner. This efficiency will be driven by innovations in manufacturing technologies, operational approaches, collaboration and digitalization, embracing the best-in-class approaches that have been developed by other industries and adapting them for our industry.

MH: Automation of manufacturing is a big driver to reduce cost and error. By introducing automation early on, developers can be better prepared to take a product into, for example, continuous manufacturing for a phase III clinical program and to easily integrate automated processes. But there are many considerations that would enable or disable the ability to produce a “lights out” factory. One I find particularly interesting is the ability to automate analysis of process parameters and product quality attributes to keep a check on quality in real-time. How would this look in a fully automated factory? Would all unit operations of a manufacturing process upstream and downstream require monitoring with multiple analytical technologies? Will this focus on a continuous manufacturing process? How would AI or machine learning be involved in this automated process analytical approach? And will AI and machine learning enable intelligent real-time decisions during manufacture? There is a great

deal of work to be done on continued improvement of analytical technologies, not just for accuracy and precision, but for robustness and intelligent implementation in control strategies.

What are the biggest challenges (for pessimists) or biggest opportunities (for optimists) when it comes to the growth of the biopharma industry?

NR: The biggest opportunity and challenge is our mindset toward adoption of new technologies and new ways of doing things. Though there may be many reasons why change is hard, change drives us toward a better future. As an industry, we need to truly measure our success through the metric of time from “idea to adoption.” Even if we make small improvements in this metric, it will have a significant impact on our whole industry.

MH: Delivering innovation is a challenge and an opportunity. Innovation is difficult. If there isn't a focus on it – meaning it has to compete with the day to day – then it will never be a priority. But I am an optimist; I see a constant focus on innovation within our company, and this is mirrored throughout the biopharma industry. Teams focused on innovation, and delivering innovation that makes positive change, will help drive collaboration and the delivery of novel discovery tools, new modalities, and improved processes in research and manufacturing. Companies need innovation teams to identify challenges and gaps – to look far and wide to identify novel solutions.

How challenging do you find workforce recruitment and development?

NR: The pandemic has significantly changed people's mindsets toward priorities in their life, and this has changed what people expect from their jobs and careers. I don't think we, as an industry, yet understand what that change is and how to address it. But we must be prepared to continue to shift our expectations and mindsets about jobs.