Debottlenecking strategies to accelerate time to market

Dr Vivek Kumar, biopharma market development manager for **Spectrum Chemical**, explores new strategies for development and speed to market, applying key learnings from the COVID-19 pandemic

Research and "Markets' '2021 Pharmaceuticals Research Review' report states that the global market for generic drugs should grow from $411.6 billion in 2020 to $650.3 billion by 2025, and identifies immunology, oncology and neurology as the fastest-growing therapy areas expected to be the main sources of growth through 2026.

The report points out the biologics market is growing at a significant rate and is projected to continue outstripping that of small molecules in the coming decade.[1] The biopharmaceuticals market was valued around $401.32 billion in 2021 and is expected to reach $534.19 billion in 2027.[2]

The unprecedented speed of COVID-19 vaccine development has immense significance for the accelerated development of new vaccines and other therapeutics, including orphan drugs. If the pandemic lessons learned by the industry are applied and incorporated into new strategies, processes and operations, it promises to transform the development of novel pharmaceuticals, biopharmaceuticals and additional therapeutics, as well as new diagnostics.

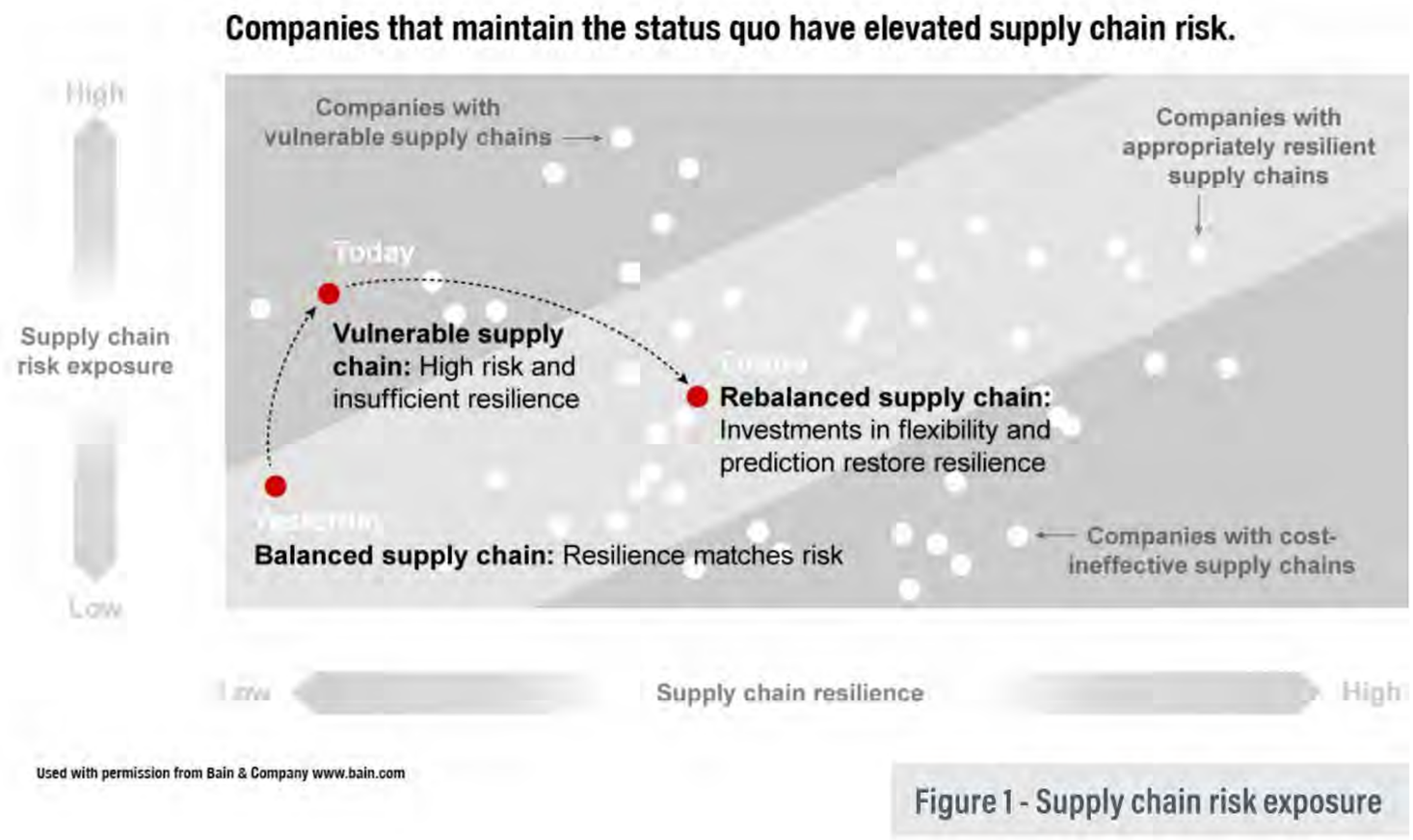

Figure 1 - Supply chain risk exposure

From just in time to just in case

Despite the progress in containing and overcoming COVID-19, many of the supply chain challenges caused by the pandemic remain. In the after-action assessment of the industry's global response to COVID-19, five trends and related strategies have emerged:

1. Ongoing planning issues, with increasingly complex supply networks
2. Sourcing verifiable high-quality raw materials in line with stringent specifications
3. Longer delivery lead times for essential product components
4. Traceability and change control issues
5. Meeting ever-increasing scrutiny and regulatory compliance requirements

The pandemic has shone an intense spotlight on the weaknesses of the global supply chain and created a new necessity to build greater resiliency and agility into supply chain management. As stated in a Bain & Company brief: "Resilient and flexible supply chains can be a powerful defensive hedge, but also a source of competitive advantage. Leaders make the most of options such as capacity buffers, digital infrastructure and nimble teams to react faster and more efficiently than their peers."[3]

Pharmaceutical and biopharmaceutical manufacturers who are proactively responding to the need for change post-pandemic are working on increasing resilience and future-oriented agility in their supply chains, recognising the importance of streamlining operations for supply chain efficiency. This includes optimising the use of raw materials from their suppliers as early as possible.

Improving efficiency requires a robust business process to identify vulnerabilities in production and the supply chain, taking into consideration both normal operations and disruption scenarios. For example, having a more resilient supply chain means moving beyond 'just in time' manufacturing to a 'just in case' inventory of critical

product components in place as a responsive stock buffer for supply chain disruptions.

Choosing the right supplier plays a key role in agility, particularly in assuring the quality of purchased materials. In addition to dependable quality of materials, the right supplier provides comprehensive documentation that meets regulatory compliance, plus additional and customised testing to help control the successful execution of the final manufactured product. Partnering with the right supplier is both cost- and time-saving in avoiding non-conformities, deviations, potential reputation damage and loss of customer confidence.

Application of AI & digital tools

There has been a significant increase in digitalisation investment in both the pharmaceutical and biopharmaceutical industries since the pandemic. Digital tools and processes provide a competitive advantage in agility and speed, increasing efficiency in operations, better data quality through virtual data access, improved R&D productivity, faster delivery of advanced therapeutics, easier compliance and less wasted product.

Deloitte shared the findings of its 2021 survey of 150 biopharma leaders to better understand the industry's approach to digital innovation in this environment of accelerated change. "Biopharma is now at a digital innovation inflection point. Organisations face an important choice: either decelerate the pace of digital innovation or pursue what we call leapfrog digital innovation," it noted.

Deloitte's survey results suggest that specific digital technologies are already widely adopted and incorporated into biopharma operations. More than a third of survey respondents reported using more digital technologies in day-to-day operations, including the cloud (49%), AI (38%), data lakes (33% and wearables (33%) in day-to-day operations.[4]

These and other technologies have enormous potential to help create a digital transformation in global drug manufacturing that can accelerate speed to innovation and commercialisation of new products that will benefit patients worldwide.

Significant competitive advantage is already with drug manufacturers that have been early adopters, recognising that the future is digital. Now, the industry as a whole understands that it is an imperative to implement strategic plans for digital innovation to succeed in the new digital economy.

Risk management & mitigation

Risk management is often referred to as 'decision-making under uncertainty'. Risk management planning seeks to improve decision-making in identifying and controlling

Figure 2 - Digital innovation in the lab

Digital innovations	Description
AI-driven drug discovery *(AI)*	• AI applied to knowledge graphs automated target identification and validation, and reduces time spent on screening of extensive molecular libraries to identify lead molecules. • AI-based computational chemistry toolkits enable discovery scientists to explore novel spaces and broaden the pool of potential structures to consider as drug candidates, increasing development pipeline size and diversity.
Automated lab processes *(robotics and IoT)*	• Physical and digital robots automate lab processes such as sample preparation, pipetting and standard analytical testing, managing these activities with high precision and repeatability, reducing manual workloads.
Virtual data assistances *(AR/VR, AI)*	• Digital assistances with AR/VR, NLP (natural language processing) and computer vision facilitate hands-free work by displaying steps of a lab procedure and notes from previous experiments while automatically recording all video and audio observations.
Interoperable data ecosystems *(IoT)*	• Through IoT, research platforms and smart instruments can automatically clean, store and upload data to cloud platforms to create an interoperable lab ecosystem. • This will ensure connectivity, access and availability of data and insights from discovery experiments when needed.
Seamless data sharing and access *(cloud)*	• Through the creation of seamless and dynamic workflows via cloud data storage, scientists across organizations and geographies can effortlessly share data collected during experiments (such as audio recordings and research notes) and work together to analyse data and strategize follow-up experiments.

Source - Deloitte

risk. To be effective, risk management must be a thorough and continuous process, an organisation-wide commitment, with responsibility coming from employees in the production suite up to the C-suite.

Biopharmaceutical development is complicated and usually lengthier than pharmaceuticals. Risk mitigation demands that the highest quality be maintained throughout the cycles of preclinical, early (Phase I-II) and late (Phase III-IV) clinical development for product quality and patient safety.

Unlike pharmaceuticals, the top risks in biopharma manufacturing are microbial contamination of in-process materials, high bioburden levels, critical component failure and supplier non-conformance. In addition to keeping development and manufacturing costs in line, the goal is safeguarding drug quality and patient safety while at the same time accelerating speed to market.

Manufacturers are required to follow ICH Q9 for QRM and ICH Q10 (1, 2) for risk oversight by senior quality management. Regulatory assessment has brought about an increased emphasis on the control and management of raw materials.

With digital tools now augmenting processes, a digitalised approach can be taken to supply chain design that will increase risk monitoring capability, thereby greatly strengthening safety, resilience and agility. More precise digital tracking and analysis of each raw material or product component will help ensure quality and avoid various supply issues.

It is obvious post-COVID that a comprehensive risk management plan includes assessing all potential challenges that can arise from supply chain disruptions, anticipating and planning for inventory levels as potential buffers, boosting agile manufacturing and identifying alternate supply sources.

Figure 3 - Top considerations for selecting a raw materials supplier

Quality management

Quality control (QC) plays a vital role in commercial innovation and achieving the goal of speeding time-to-market for medicines to be produced and distributed to patients throughout the world. Building a quality-centric company culture is key to significantly improving quality control.

For QC efforts to be effective, manufacturers must establish an all-inclusive programme that encompasses every core component of their supply chains, including integration, operations, procurement and distribution. The programme should be supported by a quality-centric company culture led from the top down.

Paramount to meeting compliance requirements, regulatory scrutiny and ensuring product safety is to ensure optimal quality and purity of the chemical ingredients, APIs and excipients used in production. In addition, the quality of raw materials and other critical components is only as good as the laboratory tests and scientific documentation supporting that they have been fully tested and traceable.

Documentation is imperative and specific products require special testing and certification for bioburden, elemental impurities or endotoxins. Thorough testing reduces process variability and increases repeatability and reproducibility to provide accurate and reliable results. Such documentation, not only on downstream production chemicals but also on materials used during pilot and scale-up phases, mitigates financial and market risk by avoiding down time, and sourcing issues as a product moves through the development process.

In conjunction with meeting regulatory demands and best practices, partnering with the right supplier who offers high-quality products and global distribution

network expertise is crucial to successfully navigating quality control challenges and developing solutions in real-time.

From 'large-large' to 'small-small'

Even before the COVID-19 pandemic, the pharmaceutical industry had been changing its focus on blockbuster drugs for common ailments that affect large populations to focusing on 'niche-busters', orphan drugs for smaller populations of patients with unmet needs for rare diseases or other underserved medical conditions.[5]

In 2021 orphan drugs accounted for 52% of the 50 novel drugs approved by the FDA's Center for Drug Evaluation & Research.[6] 21 of the 26 orphan drugs received first-in-class approvals, an indication of the strong innovation ongoing in the rare disease sector.

Several factors benefit developers of orphan drugs. The US government offers financial incentives. Drug candidates granted orphan designation often gain accelerated assessment and designated orphan drugs can receive market exclusivity for determined periods of time. The clinical trials are often smaller in size and have shorter clinical trial times, expediting regulatory approval and speeding time to market.

A significant internal factor in orphan drug development also contributes to accelerating time to market. Orphan drug R&D and manufacturing require smaller volumes of material and production sizes. As such, they can benefit from choosing the same quality of materials in their early phases as they do in production. This helps compress time-to-market because they are using the same quality of material in the early phases before moving forward with production.

An example of such raw material includes Biocertified* chemicals developed by Spectrum Chemical as part of a larger quality management programme. These raw materials undergo expanded laboratory testing, certifications and documentation to fulfill the unique requirements of each bioprocessing cycle from drug discovery to pilot and scale-up production. The high purity of materials assists in meeting regulatory and compliance requirements while reducing time to market for new drugs, vaccines and therapeutics.

The pandemic placed a demand on pharma and biopharma companies to move quickly on making changes to their commercial operating models in improving agility, efficiency and resource allocation, a demand that is ongoing. Multiple sources of technology, including new analytical tools, will offer opportunities for new partnerships and more informed customer relationship.

With the trending investment in digitalisation comes the need to integrate the new technologies into strategic planning, operating processes, as well as introducing new methods of working. Senior management needs to bring their companies forward, providing leadership and resources to achieve competitive goals. Agility and forward-thinking will contribute to innovative solutions and accelerate success in a changing marketplace.

Conclusion

The COVID-19 pandemic has ushered in a new era in drug development cand in the ways that pharmaceutical and biopharmaceutical manufacturers will operate in the future. The industry's contributions to medical discoveries and innovative medicines will mean tremendous growth and commercial success for market leaders and will bring great benefit to patients and customers on a global scale. ●

** bioCERTIFIED is a registered trademark of Spectrum Chemical Mfg. Corp.*

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References:

1: *Research and Markets, 2021 Pharmaceuticals Research Review, March 2022: https://www.researchandmarkets.com/reports/5555952/2021-pharmaceuticalspresearch[review#src-pos-1*

2: *Mordor Intelligence, Biopharmaceuticals Market – Growth, Trends, Covid-19 Impact, & Forecasts, January 2022: https://wwwmordorintelligence.com/industry-reports/global-biopharmaceuticals-market-industry*

3: *J. Hinkel, A. Thakker & R. Tsang, Shock-Proof: How to Forge Resilient Supply Chains, Bain & Company, 18 November 2020 Bain & Company Brief. Used with permission: https://bain.com/insights/shock-proof-how-to-forge-resilient-supply-chains*

4: *A. Kumala, W. Miranda, T. Konersmann & A. Israel, Biopharma digital transformation: Gain an edge with leapfrog digital innovation. Deloitte Development LLC December 2021: https://www.deloitte.com/global/en/insights/industry/life-sciences/biopharma-digital-transformation.html*

5: *T. Yang, Biopharma Business Models 2040, Deloitte Consulting, 31 March 2020: https://www2.deloitte.com/us/en/blog/health-care-blog/2020/biopharma-business-models.html*

6: *Global Genes, 12 January 2022: https://globalgenes.org/2022/01/12/a-group-of-innovative-orphan-drugs-win-fda-approval-in-2021/?gclid=Cj0KCQjwzqSWBhDPARIsAK38LY9-0fUXNy_hbZhALGGP0MzvAoCj4QEAXNeVaP0j5CiHlhtWFgC3g8kaAt0qEALw_wcB*