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Biopharma manufacturing scale-up

Applying right capabilities to drive right-first-time execution at scale



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Abstract

Biopharma manufacturing scale-up has become an important leadership priority because installed capacity creates value only when it can be converted into reliable, right-first-time production.

As demand increases across complex therapies, sterile products, biologics, and emerging modalities, manufacturers can no longer treat scale-up as a technical milestone that follows equipment installation, commissioning, or validation planning. Manufacturing ramp-up increasingly depends on the coordinated performance of network planning, site leadership routines, frontline execution, data visibility, workforce readiness, and quality discipline under real production pressure.

Many manufacturing organizations can stabilize operations through short-term interventions, but stabilization alone does not create sustainable scale. Foundational capabilities, such as daily issue containment, rapid problem-solving, and short-cycle operational support, remain essential during startup and early ramp-up because manufacturing teams must maintain continuity while the operating environment matures. However, foundational capabilities become insufficient when production expectations rise, recurring sources of variability persist, and cross-functional decisions need to be made with speed and consistency. Sustainable scale requires enduring capabilities that strengthen the operating system, including process excellence, trusted performance data, effective tools and technology, clear operating model routines, and workforce capability that extends beyond procedural compliance.

The central point of view of this white paper is that right-first-time scale-up depends on a complementary set of capabilities rather than a single intervention, tool, or implementation plan. Foundational capabilities help manufacturing sites stabilize daily operations, while enduring capabilities help those sites sustain performance as volume, complexity, and production expectations increase. Manufacturers that deliberately build both capability sets can reduce execution variability, improve operational readiness, shorten the path to reliable output, and strengthen the role of scale-up in supporting patient access, supply resilience, and commercial performance.



CHAPTER 1:

The strategic imperative to scale up right the first time

Recent shortage patterns across high-growth and complex product categories demonstrate how quickly patient demand can place pressure on existing manufacturing and supply networks. American Society of Health-System Pharmacists (ASHP) and the University of Utah Drug Information Service reported 223 active drug shortages as of March 2026,[1] below the first-quarter 2024 peak of 323 but still indicative of continued pressure across the US drug supply system. For biopharma manufacturers, the shortage environment reinforces a practical operating reality: supply reliability depends not only on installed capacity, but also on the ability to bring capacity online with consistency, quality, and speed.

223 active drug shortages, Q1 2026[2]

Despite easing from the 2024 peak of 323 cases, shortages remain historically high, showing that manufacturing networks have yet to regain resilience

~56% of new shortages are injectables[3]

Parenteral products dominate new shortages, driven by aseptic fill-finish complexity, sterility assurance, and component constraints

Manufacturing accounts for 38% of known issues[4]

Of the cases where causes are disclosed, nearly 4 in 10 links to manufacturing issues, underscoring how right-first-time production is central to improving supply reliability

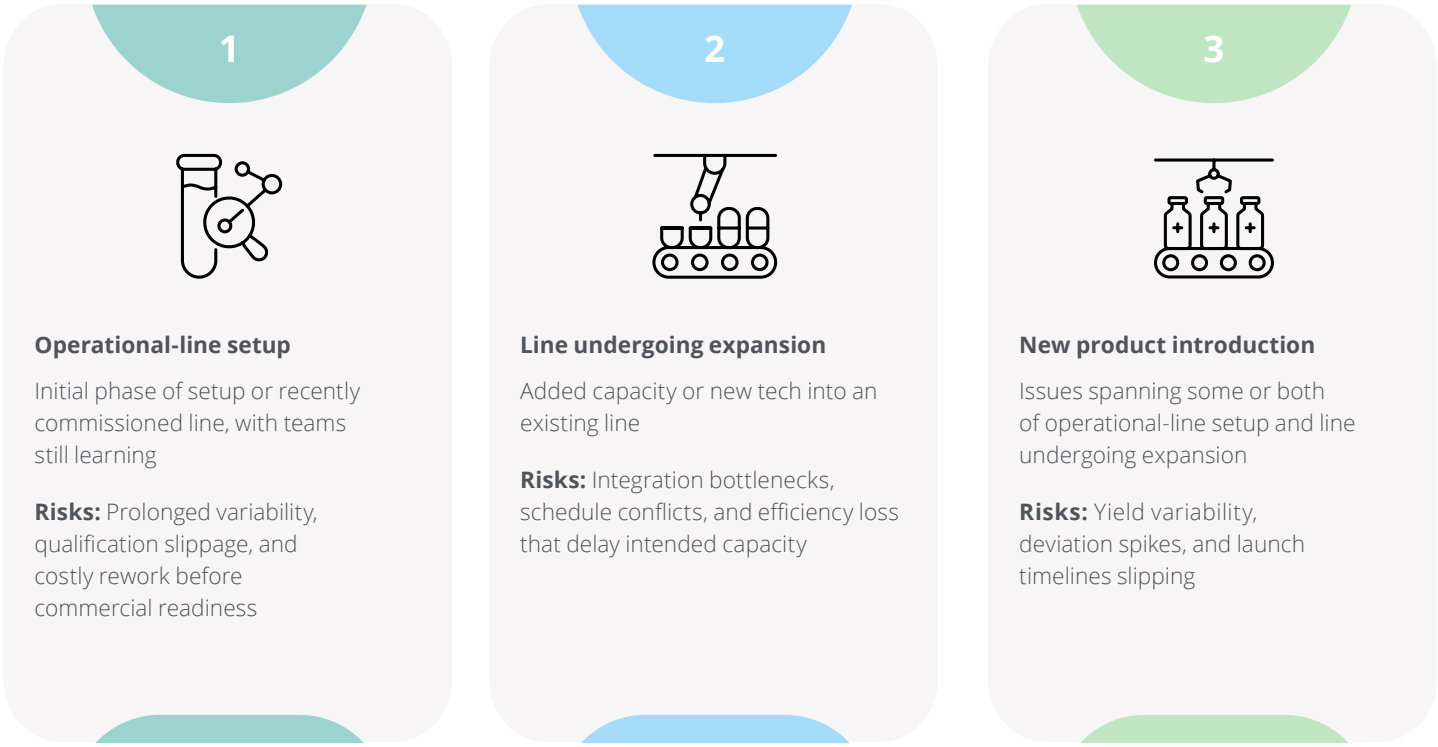
The scale-up imperative is becoming more relevant as manufacturers invest in new sites, line expansions, and equipment installations to support evolving portfolios and future demand. New capacity can strengthen supply resilience, but production networks realize the benefit of that investment only when assets move from construction, commissioning, and qualification into stable operational performance. The composition of recent shortages further underscores the importance of execution in complex modalities, particularly parenteral products, where aseptic fill-finish, sterility assurance, component availability, and controlled production environments create additional operating requirements. Manufacturing-related issues also account for a meaningful share of disclosed shortage causes, suggesting that production readiness, process reliability, and right-first-time execution remain central contributors to supply assurance.

Against this backdrop of persistent shortages and growing supply pressures, leading manufacturers are expanding capacity at unprecedented scale. In 2024–2025,

- Lilly announced four new US manufacturing sites, three focused on API production and one on parenteral medicines to stay ahead of anticipated demand;[5]
- Merck broke ground on a $3 billion, 400,000-square-foot center of excellence for pharmaceutical manufacturing in Elkton, Virginia, adding both active pharmaceutical ingredients and drug product capacity for small molecule production to strengthen domestic supply;[6] and
- Fujifilm raised its investment in its CDMO campus in Holly Springs, North Carolina, to more than $3.2 billion, adding eight 20,000-liter bioreactors to strengthen supply chain resilience and address growing outsourcing requirements.[7]

Manufacturing scale-up becomes critical when market demand, patient need, or launch commitments require production networks to move from planned capacity to reliable output. Scale-up typically emerges through three operating scenarios as depicted in figure 1: an operational-line setup, a line undergoing expansion, or a new product introduction.

Figure 1.



Each scenario carries a distinct risk profile, from learning-curve effects and qualification slippage in newly commissioned lines, to integration bottlenecks in expanded lines, to process-transfer, validation, quality, and launch-timeline risks in new product introductions. Manufacturing leaders should therefore begin scale-up planning by diagnosing the operating scenario, identifying the primary sources of execution risk, and understanding the challenges that surface during ramp-up before selecting the capabilities, investments, and interventions required for right-first-time execution.

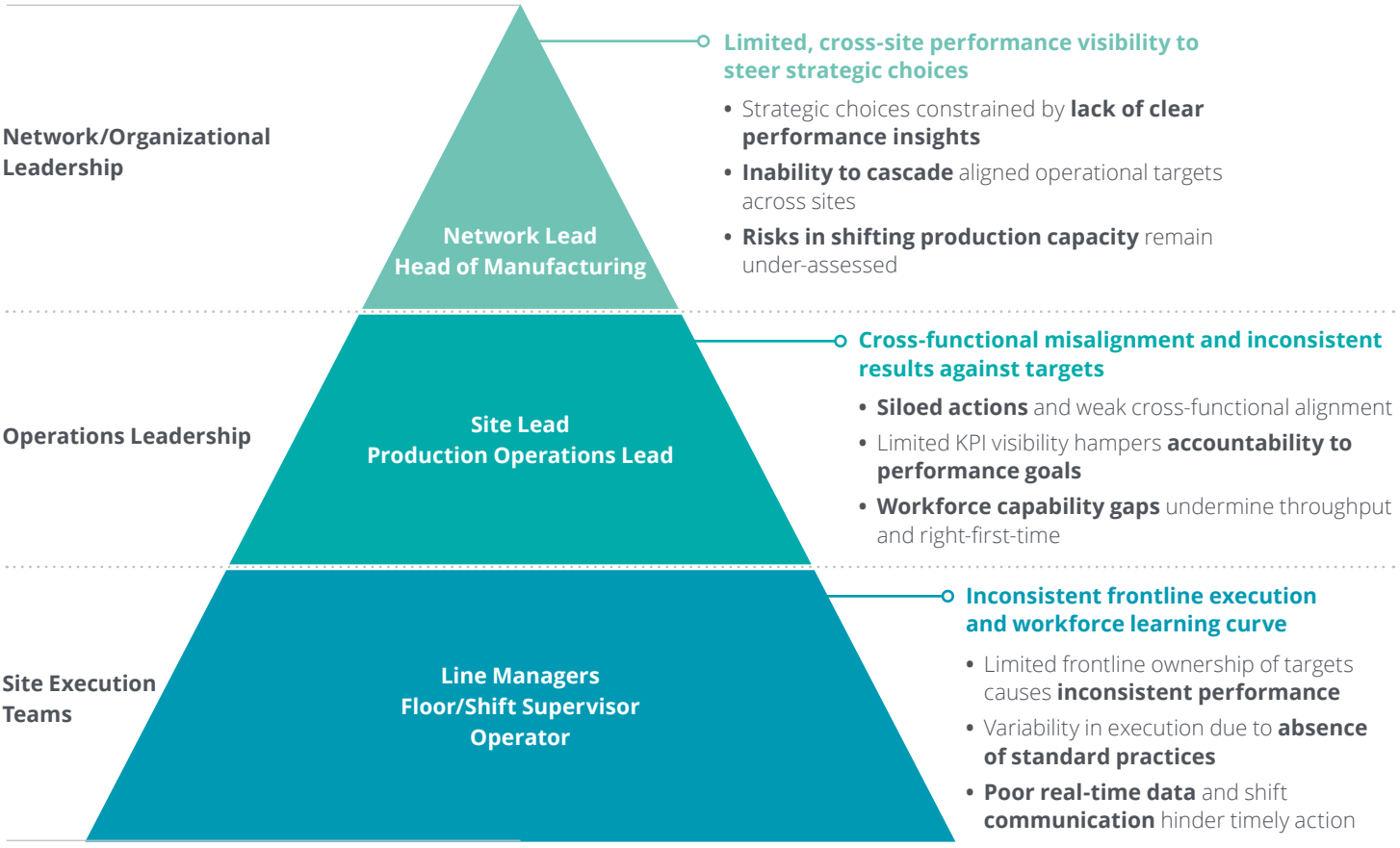
CHAPTER 2:

Scale-up challenges across the organization

Scale-up pressure usually becomes visible on the manufacturing floor, but the underlying causes of scale-up variability often extend across the organization. Inconsistent output, qualification slippage, downtime pressure, and deviation recurrence may appear to be line-level problems, yet those symptoms frequently reflect gaps in network visibility, operational governance, data quality, workforce capability, or frontline execution discipline. Manufacturing ramp-up must therefore be understood as an enterprise operating-system challenge.

Manufacturing scale-up challenges manifest across three levels of the organization (figure 2): network or organizational leadership, operations leadership, and site execution teams.

Figure 2.



At the network leadership level, scale-up performance depends on the quality of strategic visibility. Network leaders need a clear view of demand, capacity, ramp-up risk, site maturity, and cross-site learning opportunities. Incomplete performance insight can constrain decisions about capacity allocation, production shifts, resource deployment, and risk mitigation. A network leader may know that a site is behind its ramp-up trajectory, but may not know whether workforce readiness, equipment reliability, process variability, quality events, material constraints, or support-function gaps are driving the performance shortfall.

At the operations leadership level, scale-up performance depends on the ability to translate enterprise priorities into aligned execution. Manufacturing leaders must cascade targets, coordinate functions, clarify ownership, and ensure that meeting routines produce decisions rather than only updates. Weak operational governance can allow functions to work hard without working in concert, while limited KPI visibility can reduce accountability against performance goals. Under scale-up pressure, fragmented governance creates activity without adequate control.

At the site execution level, scale-up performance depends on the consistency of daily work. Operators, supervisors, line managers, and support teams require clear standards, practical job aids, reliable shift handovers, timely data, and escalation pathways that support fast, disciplined response. Workforce learning-curve constraints, inconsistent standards of work, weak communication channels, and limited frontline ownership of targets can create variation across shifts and teams. Repeated variation at the execution level can undermine even well-designed network and site plans.

The interaction among organizational levels explains why isolated fixes may not sustain scale-up improvement over time. Network scorecards have limited value when frontline teams do not have sufficient confidence in the data or clarity on the expected response. Frontline routines can improve local execution, but local routines may not address broader constraints without operations leadership involvement. Operations governance can create management cadence, but cadence alone does not improve outcomes without a reliable fact base and clear follow-through. Sustainable scale therefore requires the three levels of the organization to reinforce one another through shared visibility, aligned governance, and consistent execution. The management's task is to build complementary capabilities that address both needs: foundational capabilities that stabilize daily operations, and enduring capabilities that strengthen the operating system required for scalable performance.



CHAPTER 3:

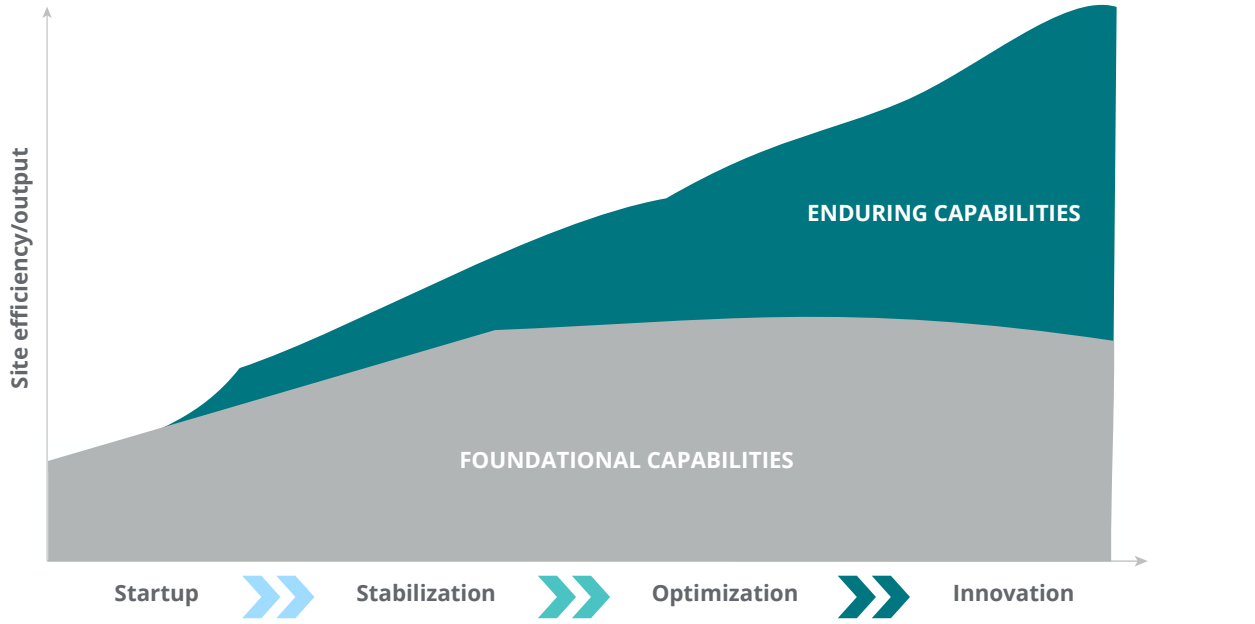
Building complementary capabilities

Every scale-up journey requires foundational capabilities because early-stage operations must maintain continuity while uncertainty remains high. Foundational capabilities include daily management routines, short-cycle problem-solving, rapid issue containment, and the practical coordination needed to keep production moving while equipment, processes, and teams mature. These capabilities are necessary because durable improvement cannot be built on an unstable operating foundation.

Foundational capabilities, however, can create a false sense of progress when reactive stabilization becomes the organization's default way of working. A site may recover from downtime, complete batches, close deviations, or meet a short-term output target while still relying on temporary staffing, manual workarounds, exclusive leadership attention, or a small group of highly experienced individuals. Under those conditions, the site has protected initial production volume, but the underlying system may still be unprepared for higher volumes, longer campaigns, or more complex product requirements.

Foundational capabilities secure short-term continuity, but only **enduring capabilities move sites beyond stabilization** to sustainable scale

Figure 3.



Enduring capabilities complement foundational capabilities by strengthening the operating system that produces performance. Enduring capabilities are longer-cycle, proactive, and improvement-focused disciplines that help organizations identify root causes, standardize execution, sustain countermeasures, improve workforce effectiveness, strengthen data quality, and prevent regression after early gains. The role of enduring capabilities is not to replace daily management, but to reduce the amount of firefighting required to sustain output.

The balance between foundational and enduring capabilities should shift as the site matures. Startup environments typically require strong foundational routines because immediate stability is the priority. Stabilization creates the window to introduce enduring capabilities that address recurring failure modes. Optimization depends increasingly on enduring capabilities because the site must improve throughput, reduce variability, and sustain quality without disproportionate management intervention. Innovation becomes possible when enduring capabilities support digital integration, continuous improvement, and scalable learning.

The management implication is that stabilization should be treated as a platform rather than an endpoint. A site becomes scalable when reliable output is sustained through standard work, trusted data, clear governance, and capable teams rather than through repeated escalation. The practical question for leaders is not whether foundational or enduring capabilities matter more. The higher-value question is when enduring capabilities should begin carrying more of the performance burden.

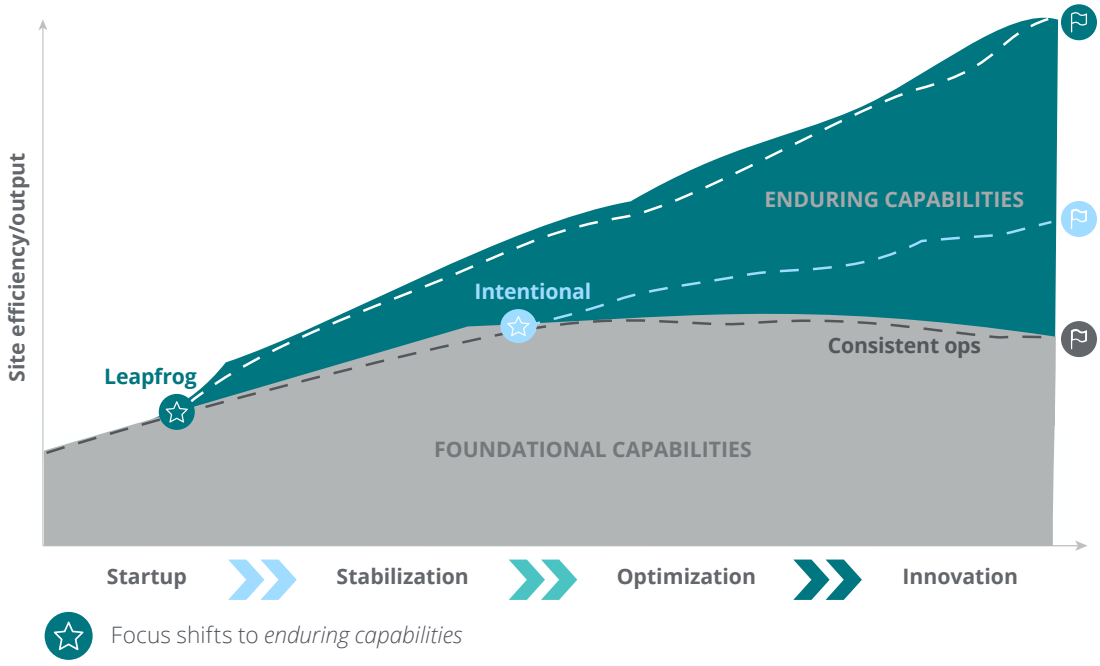


CHAPTER 4:

Choosing the right scale-up path

Biopharma manufacturers should not apply a uniform scale-up approach across all sites, products, or lines. The appropriate path depends on demand certainty, production urgency, patient criticality, site maturity, workforce readiness, and the consequences of delayed or inconsistent output. A site serving uncertain demand may require a different capability sequence from a site supporting a high-demand or patient-critical product. The scale-up path determines how quickly enduring capabilities should be introduced and how much dedicated support the site may need (figure 4).

Figure 4.



A. Consistent operations

The *consistent operations* path is most appropriate when baseline production is required but demand remains uncertain or production urgency is moderate. *Consistent operations* emphasizes stability routines, daily management discipline, issue containment, and reliable execution of core activities. The path can help a site establish a predictable operating baseline, which is necessary before more advanced capability building can take hold. The limitation is that a stability-led path can create a lower performance ceiling when leaders do not introduce the capabilities required to improve throughput, reduce recurring losses, and prepare for higher demand.

B. Intentional scale-up

The *intentional scale-up* path is most appropriate when production needs are moderate and demand is emerging. *Intentional scale-up* begins with stabilization and introduces enduring capabilities in a sequenced manner as the site matures. The path allows teams to absorb new routines, develop skills, refine governance mechanisms, and embed standard ways of working without overwhelming the organization. The primary constraint is speed because a sequenced capability agenda may not move quickly enough if demand accelerates faster than expected or if patient and commercial risks increase.

C. Leapfrog scale-up

The *leapfrog scale-up* path is most appropriate when production needs are high, demand certainty is strong, and delayed ramp-up would create meaningful patient, supply, or commercial risk. *Leapfrog scale-up* embeds enduring capabilities from startup with dedicated support, allowing the organization to address drivers of variability before firefighting becomes the default operating model. The path can accelerate the journey to peak performance, but early capability investment requires disciplined prioritization, strong leadership alignment, and careful attention to the frontline capacity required to absorb change.

The three paths should be viewed as strategic choices rather than maturity labels. The faster a site must scale, and the more certain or critical the demand is, the earlier leaders should embed enduring capabilities. When demand remains uncertain, leaders may choose a stability-focused path while preparing to add scalability capabilities as demand clarifies. Scale-up strategy should therefore reflect the site's business context, not a generic sequence of improvement activity.

CHAPTER 5:

Four capability levers that enable right-first-time scale-up

Once leaders select the scale-up path, the next decision concerns where capability-building effort should be focused. In figure 5, four levers provide a practical structure for diagnosing the drivers of scale-up variability and prioritizing interventions: process excellence, tools and technology, data management, and talent and operating model. These levers are not independent workstreams. The levers create impact when they operate as an integrated capability agenda that connects how work is designed, how technology supports execution, how performance is measured, and how people act on the operating model.

Figure 5.



Process excellence

Process excellence reduces variability by standardizing how work is performed across processes, shifts, and teams. In scale-up environments, unclear standards of work, incomplete readiness for media fills, process validation, or campaign extensions can create delays, rework, and recurring issues. The objective of process excellence is not additional documentation. The objective is reliable execution through standard work, process deep dives, bottleneck analysis, root-cause countermeasures, campaign-break analysis, and readiness checks at stage gates.

Tools and technology

Tools and technology enable scale-up when systems, equipment, and digital workflows make work more reliable at the point of need. Manufacturing execution systems, downtime tracking tools, digital handover boards, validated job aids, equipment reliability tools, and cross-site knowledge-transfer platforms can improve execution only when operators can use them confidently and leaders can trust the information generated. AI-enabled capabilities can further support targeted use cases, such as downtime pattern recognition, deviation trend analysis, and faster retrieval of cross-site learnings. The FDA defines advanced manufacturing as "a collective term for new or innovatively applied medical product manufacturing technologies that can improve drug quality, address shortages of medicines, and speed time-to-market."[8] Technology adoption therefore matters, but value depends on usability, validation, trusted data, and integration into daily routines.

Data management

Data management gives leaders a timely, trusted, and actionable view of performance. Scale-up environments often suffer when critical metrics are late, inconsistent, manually reconciled, or disconnected from decisions. A stronger data foundation creates a single source of truth, clear KPI ownership, timely production monitoring, leadership scorecards, batch-time diagnostics, loss analytics, and throughput analytics. Research on machine learning in biopharmaceutical process development and manufacturing highlights the relevance of advanced analytics for monitoring, control, and optimization, while also noting challenges related to data complexity and implementation. Advanced analytics therefore require disciplined data foundations before broader adoption can create reliable value.

Talent and operating model

Talent and operating model capabilities determine whether plans, tools, and data translate into consistent daily execution. Scale-up often exposes gaps in roles, decision rights, meeting governance, escalation routines, shift handovers, and operator depth. A stronger talent and operating model agenda includes operator upskilling, role-based training, shift handover routines, job aids, escalation matrices, parts readiness, maintenance coordination, and clear ownership for tiered performance management. Workforce capability should be measured not only by procedural qualification, but also by the ability to execute confidently under production pressure.

Capability lever	Typical challenge	Prospective solution areas
 **Process excellence**	• Unclear standards of work create variability across shifts and teams • Sites are not prepared/lack visibility to failure modes for scenarios such as media fill, process validation (PV), and campaign extensions	• Standard work, process deep dives, root-cause countermeasures, campaign break analysis, readiness checks
 **Tools and technology**	• Technology systems are underutilized, and manual workarounds dominate core workflows • Operators are not fully versed in critical equipment platforms (e.g., MES), creating key-person dependency and unplanned downtime	• Downtime tracking, digital handover boards, MES enablement, equipment reliability tools, knowledge-transfer platforms
 **Talent and operating model**	• Tier meetings, shift handovers, and communication channels are weak, leading to misalignment and slow issue escalation • Operators are insufficiently qualified and lack the required depth for critical tasks	• Operator upskilling, role-based training, meeting governance, escalation matrices, job aids, parts readiness
 **Data management**	• Critical metrics are inconsistent or late, and insights do not translate into timely, accountable action • Absence of single source of truth, with operations heavily relying on unconnected spreadsheets	• Production monitoring, leadership scorecards, batch-time diagnostics, loss analytics, KPI ownership routines

The four levers should be deployed together rather than treated as a menu of unrelated initiatives. Process discipline is difficult to sustain without trained teams and clear governance. Technology has limited value without trusted data and consistent adoption. Data visibility does not improve performance unless leaders act on the insights. Workforce investments lose impact when work standards and escalation pathways remain unclear. The strongest scale-up programs therefore integrate the four levers into a coherent operating system.

What's next for accelerating your manufacturing scale-up

The path forward should begin with a focused leadership diagnosis rather than a broad solution launch. A disciplined diagnosis helps leaders determine whether the scale-up plan is realistic, which path fits the site's context, which capabilities require immediate investment, and which operating gaps could slow the journey to reliable output.

The questions below can help leaders identify where focused action can most improve right-first-time execution and accelerate sustainable scale.

1. Are our current scale-up timelines aligned with the urgency of market demand and patient needs?
2. Do we know which capabilities are needed and which path to take as we scale our manufacturing to meet our demand?
3. Is our workforce equipped with the right training, tools, and governance to deliver right-first-time execution at scale?
4. How well are we leveraging data and performance insights to identify bottlenecks and guide decisions?
5. What bold steps can we take now to transform scale-up into a competitive advantage?

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