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Bioproduction Capacity

Continual Expansion To Meet Increasing Demands

by Yasmin Timol; and Andrew B. Harmon, Tianna Goodermote, Brittany A. Martínez, Lauren Schoukroun-Barnes, Christopher Peterson, and Joseph Rininger



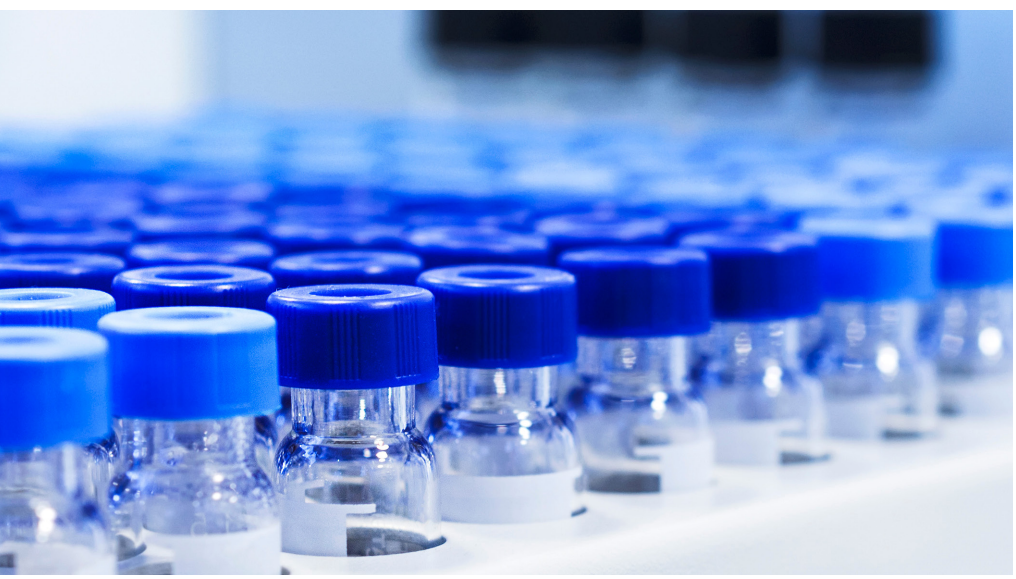
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As demand for innovative, life-saving therapeutics rises, biomanufacturers must continue to increase their own capacities to deliver such therapeutics while maintaining quality and efficacy. However, what may seem straightforward becomes complex when projected trajectories are interrupted by funding issues and global events. Thus, companies must plan and carry out capacity expansions accordingly to delivery products.

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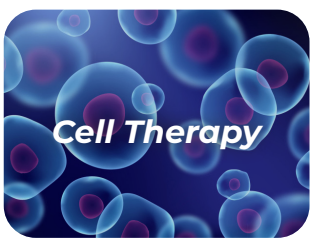
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Capacity Constraints Outpace Biomanufacturing Expansion

Yasmin Timol

Despite aggressive global expansion plans across all major biomanufacturing platforms, 30.4% of commercial production facilities report operating under "significant" or "severe" capacity constraints, a figure three times higher than that reported by early clinical manufacturers, according to the BioPlan Associates *22nd Annual Report and Survey of Biopharmaceutical Manufacturing Capacity and Production* (**1**). The report surveyed over 330 biomanufacturers and suppliers worldwide.

The data reveal a growing imbalance between investment and execution. Although facilities project average five-year capacity increases of over 30% for mammalian expression systems, and over 23% for cell, gene, and microbial platforms, key operational bottlenecks remain unresolved. Purification during downstream processing (DSP) is under pressure: Serious DSP bottlenecks have risen sixfold since 2024, with chromatography and depth filtration cited as top limitations. At the same time, the United States is outpacing Western Europe by >20% in expansion efforts, particularly for gene therapies, yet US respondents also report the highest rates of constraint severity. Those figures point to an industry at a crossroads, building more capacity than ever before but struggling to make it fully operational at commercial scale.

Mammalian Production Holds Strong, Advanced Therapies Stabilize

Mammalian cell culture continues to dominate global biomanufacturing expansion plans. According to BioPlan's report, respondents report capacity increases in mammalian culture systems that averaged 31.2% over the next five years, a value that cements the platform's central role in commercial and clinical bioproduction pipelines (Figure 1). That growth reflects both sustained demand for monoclonal antibodies (mAbs) and the maturity of related bioprocessing infrastructure.

By contrast, expansion forecasts for cell and gene therapy (CGT) platforms, which were once the industry's most aggressively expanding modalities, have begun to stabilize. Although still significant, projected capacity growth for cell therapy has dropped to 23.9% in 2025, down from 30.4% in 2024 and 38.8% in 2023.

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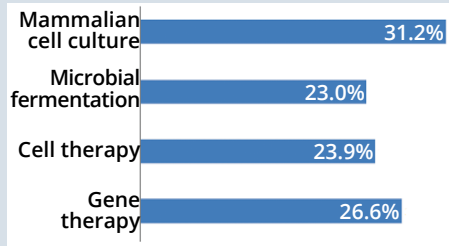
Gene therapy shows a similar trend, with expected expansion at 26.6% in 2025 compared with 28.6% in 2024 and 30.3% in 2023. However, that moderation does not signal a withdrawal from advanced therapies. Rather, it likely indicates that many facilities already have built the necessary clinical-stage capacity or sponsors have secured reliable access through partnerships with contract development and manufacturing organizations (CDMOs). The current focus is shifting toward optimizing existing capacity, navigating regulatory complexity, ensuring scalability, and aligning infrastructure with realistic commercial timelines.

Expansion expectations for microbial fermentation also have remained relatively stable. The projected 23.0% growth for 2025 reflects a gradual tempering of investment enthusiasm after a period of sharper growth (27.3% in 2024, 28.7% in 2023), suggesting a shift in strategic priorities.

Across modalities, the industry is undergoing a qualitative transformation. BioPlan's report notes that such a transformation is "a shift from 'building more' to 'building better, faster, and more adaptable'" (**1**). That emerging mindset favors modularity, agility, and targeted infrastructure investments over wholesale capacity increases.

Taken together, the data suggest that although platform-specific dynamics differ, a broader strategic evolution is underway. Organizations are recalibrating their growth strategies — not just expanding capacity, but engineering efficient, resilient systems to match the complexity and maturity of today's pipelines.

Figure 1: Average capacity increase by industry system



United States Leads the World in Capacity Expansion

Biomanufacturing capacity is expanding globally, but no region is moving as aggressively as the United States. The data from BioPlan's report show that US-based facilities are outpacing their global counterparts in both ambition and execution, particularly for gene therapy. That surge reflects several strategic drivers: the country's robust biotechnology-investment ecosystem, its access to venture and government capital, and the presence of a well-established innovation pipeline. In particular, US manufacturers appear more willing than their European counterparts to invest in large-scale infrastructure for next-generation therapies, especially where early clinical success and regulatory momentum are already visible.

By contrast, Western Europe is taking a more measured approach, concentrating expansion plans on traditional mammalian systems with a slower uptake in advanced-therapy

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manufacturing. That approach may reflect more conservative regulatory environments, cost-control pressures within national healthcare systems, or the comparatively smaller size of Europe's early stage biotechnology sector.

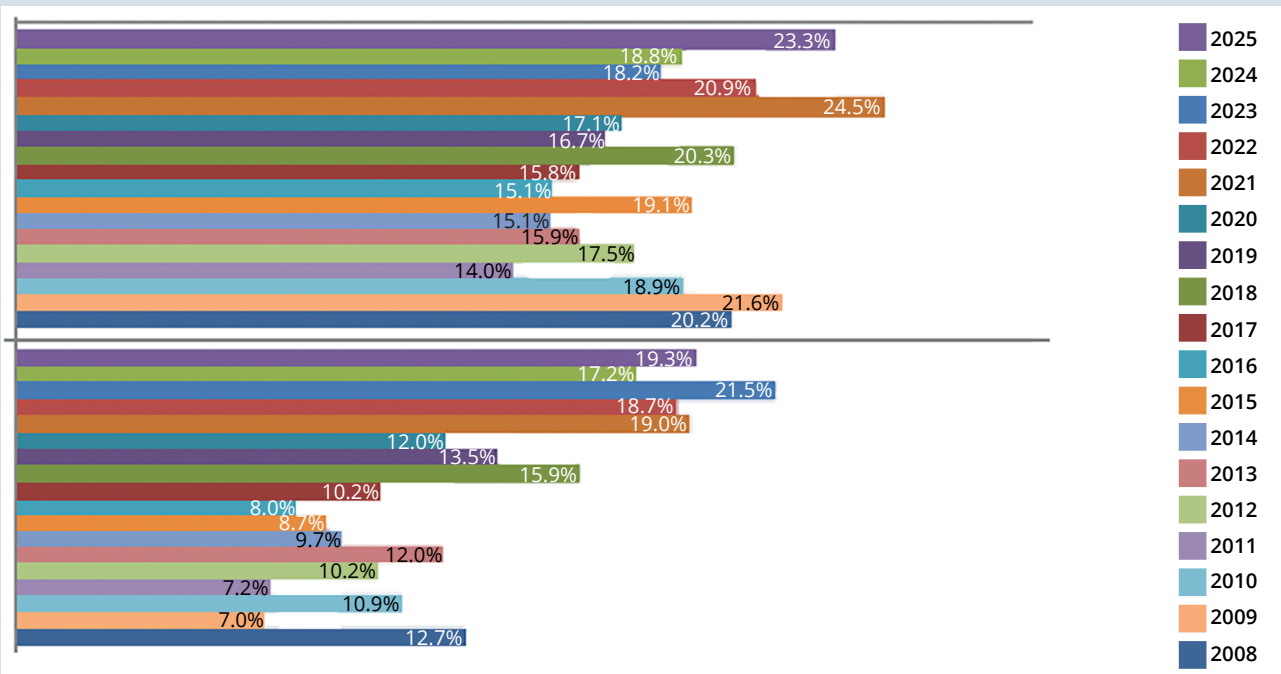
However, increasing expansion in the United States is accompanied by growing operational strain. The report highlights that US-based facilities face significantly more frequent capacity issues (≈10% more) than their Western European peers. That imbalance shows that the rapid expansion may not be matched by parallel improvements in process optimization, staffing, and/or downstream capabilities.

The data instead suggest a complex dynamic: The United States leads in capacity growth, particularly in gene therapy, but that leadership comes with growing pains. Without corresponding investments in system efficiency and bottleneck resolution, some of that new capacity will remain underused or inefficiently deployed. As other regions watch and learn from the US experience, striking the right balance between speed and business sustainability will be a defining challenge in the next phase of global biomanufacturing evolution.

CMOs and Biomanufacturers Under Pressure

Although regional differences in expansion plans are shaping the global biopharmaceutical landscape, another divide is emerging

Figure 2: Capacity of chromatography columns (TOP) and depth-filtration devices (BOTTOM) experiencing either "significant" or "severe" constraints



between contract manufacturing organizations (CMOs) and in-house biomanufacturers. The latest BioPlan data reveal a notable asymmetry in how those two groups experience capacity constraints, an imbalance that speaks to deeper structural and strategic differences in how manufacturing is organized across the industry.

CMOs, whose business models center on flexibility and scale, appear to be operating with more capacity and fewer operational bottlenecks. According to the report, 33% of CMOs report no capacity constraints, compared with 19.4% of in-house biomanufacturers. That value could reflect not only the scale of investment that CMOs are making to attract a diverse clientele, but also their investment in modular, platform-agnostic production models that allow for quick adaptation to fluctuating demand.

By contrast, in-house manufacturers (especially those scaling new therapies or moving into late-stage production) face more acute pressures. Such companies often operate within tighter resource constraints and can lack flexible infrastructure or experienced technical staff to absorb production variability. As demand for commercial-scale biomanufacturing grows, so do the structural limitations facing those facilities.

The issue is particularly pronounced in commercial manufacturing, which remains the industry's most capacity-constrained production phase. The report notes that nearly 33% of surveyed commercial-manufacturing facilities indicated that they are operating with significant capacity constraints. That number is threefold higher than it is for early stage clinical manufacturers that experience capacity constraints.

Such findings underscore a strategic vulnerability: As products move through the pipeline and regulatory approvals accelerate, many organizations are struggling to transition from clinical-scale to reliable commercial-scale output. Without targeted investment in capacity and process optimization, product-launch timelines and patient access are increasingly at risk.

Hidden Limits on Biomanufacturing Growth

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Even as biomanufacturers expand capacity and shift toward more intelligent infrastructure planning, DSP bottlenecks continue to undermine operational efficiency across the board. Despite decades of innovation upstream, DSP remains a chronic pain point in the global biomanufacturing value chain.

According to BioPlan's latest survey, the prevalence of downstream-related constraints has surged dramatically in the

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past year. The data show a nearly sixfold increase in respondents reporting "serious bottlenecks" caused by DSP systems compared with reported bottlenecks in 2024 (Figure 2). That spike reflects mounting pressure on purification systems that are struggling to keep pace with increased upstream productivity and more complex molecule types.

Chromatography systems were cited as having the highest effect on capacity limitations, followed closely by depth-filtration technologies, which accounted for 19.3% of capacity-related issues. Those steps are foundational in protein purification, and inefficiencies here can ripple throughout the entire manufacturing timeline. Such bottlenecks can lead to longer production cycles, increased cost per gram of product, and ultimately, delays in time-to-market. For companies operating in fast-moving markets, especially competitive biologics or personalized therapies, such delays can lead to lost revenue, missed regulatory windows, and reduced patient access. The issue is not simply about equipment capacity; it reflects a deep need for process integration, automation, and system-level optimization. As upstream titers rise and batch sizes grow, downstream systems must evolve to handle larger loads efficiently, consistently, and without compromising product quality.

Solving DSP bottlenecks will require more than capital investment; it requires innovation in resin technologies, filter designs, and continuous processing, as well as improved coordination between upstream and downstream operations. For many companies, addressing downstream constraints will be key to unlocking the full value of their expanded production footprints and delivering faster, more reliable biomanufacturing.

The annual report from BioPlan Associates reveals a biomanufacturing landscape in transition. Although capacity continues to expand, driven by strong investment in mammalian expression systems and sustained momentum in advanced modalities, the growth is far from uniform. The United States is accelerating ahead, especially in gene therapy, whereas Western Europe has adopted a more measured pace. At the same time, in-house biomanufacturers and commercial-scale facilities face mounting operational pressures, and downstream bottlenecks continue to limit efficiency and delay delivery.

Such findings highlight a maturing industry learning to balance ambition with pragmatism. Expansion alone is no longer the benchmark of progress; adaptability, optimization, and system-wide coordination also are now critical success factors. As stakeholders look ahead, resolving bottlenecks and investing

strategically across the production life cycle will be essential not only to capitalize on new capacity, but also to ensure that innovation translates efficiently to accessible, life-saving therapies.

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About the Author

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Viral-Vector Manufacturing Capacity and Demand

Industry Transformation and Strategic Outlook

Andrew B. Harmon, Tianna Goodermote, Brittany A. Martínez, Lauren Schoukroun-Barnes, Christopher Peterson, and Joseph Rininger

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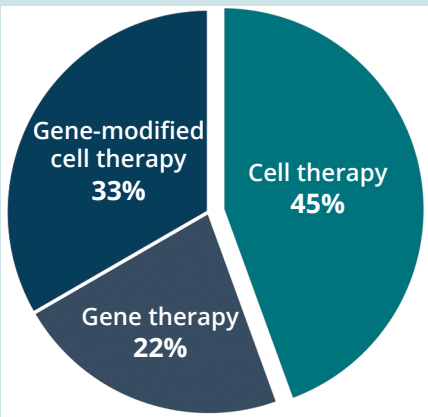
As of 15 May 2025, the US Food and Drug Administration (FDA) has approved 45 cell and gene therapy (CGT) products (Figure 1) (**1**). The European Medicines Agency (EMA) has granted centralized authorization for 20 CGT products, also termed advanced-therapy medicinal products (ATMPs) (**2**).

Cell therapies use unmodified living cells as primary therapeutic agents; such cells are used in forms including autologous and allogeneic immune effector cells, cancer vaccines, hematopoietic stem cells, and differentiated adult and embryonic stem cell preparations. For the purposes of the analysis herein, *gene therapies* consist of the direct administration of a DNA/RNA payload as the therapeutic agent, whereas *gene-modified cell therapies* consist of ex vivo genetically modified cells that subsequently are administered to patients.

Gene and gene-modified cell therapies predominantly leverage viral vectors as delivery vehicles for replacement or modification of disease-causing or defective genes. The most common viral vectors for gene therapies include adenoassociated viruses (AAVs), adenoviruses (Ads), and oncolytic viruses, whereas gene-modified cell therapies commonly involve lentiviruses and gamma retroviruses. Among those platforms, oncolytic viruses represent an emerging therapeutic class that differs fundamentally from other gene-delivery vectors. Oncolytic viruses combine payload delivery with direct tumor-cell destruction and immune-system activation and can be dosed repeatedly as a treatment regimen. Those properties position oncolytic vectors (e.g., herpes simplex virus, Ad, reovirus, and vaccinia virus platforms) as distinct therapeutic modalities that could expand treatment paradigms beyond conventional gene-replacement approaches through the potential combination with gene-modified cell therapies (**3**).

Given the critical role of viral vectors in advancing such promising therapeutics, understanding current and future market

Figure 1: Breakdown of US Food and Drug Administration (FDA)–approved cell and gene therapy (CGT) products by therapy type



demand and production capacity provides essential strategic intelligence for an industry undergoing significant transformation. We conducted an in-depth analysis using clinical-trial databases and industry data sources to evaluate clinical and commercial pipeline activity and to translate such activity into viral-vector demand projections. Primary research and industry data were used to evaluate current manufacturing capacity across contract development and manufacturing organizations (CDMOs), academic institutions, and innovator in-house facilities, providing insights into an evolving market landscape characterized by capacity expansion that has outpaced demand growth.

Historical Market Assessment

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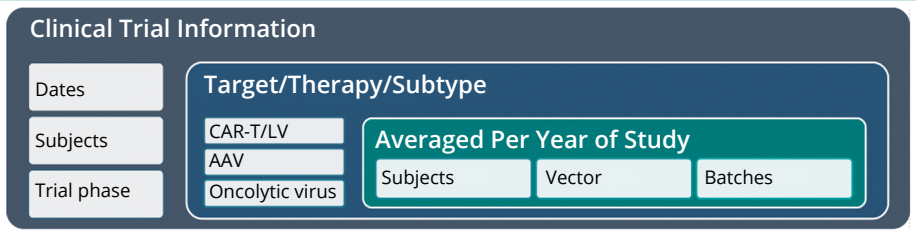
We previously conducted a viral-vector manufacturing demand and capacity analysis to provide projections for future manufacturing needs to support CGT development (**4**). That work used historical clinical-trial data from 2010 through 2018 to forecast clinical trials and subject enrollment from 2019 to 2026, translating those demands into manufacturing batch demand to assess supply requirements. The analysis projected that, by 2020, viral-vector demand would match available CDMO capacity, with demand exceeding capacity thereafter. However, unforeseen macroeconomic factors and market disruptions (e.g., the COVID-19 pandemic) fundamentally altered the anticipated path.

Our projections were made during a period of unprecedented growth and optimism in the CGT sector, driven by landmark approvals that established a regulatory framework for CGT product licensure. Key milestones included Kymriah (tisagenlecleucel) and Yescarta (axicabtagene ciloleucel) in 2017 as the first chimeric antigen receptor (CAR)–T therapies for previously intractable cancers. Similarly, Luxturna (voretigene neparvovec-rzyl) in December 2017 for rare inherited blindness and Zolgensma (onasemnogene abeparvovec) in May 2019 for fatal spinal muscular atrophy were approved. Such breakthrough therapies demonstrated compelling commercial viability — Kymriah achieved 266% growth in one year (**5, 6**), Zolgensma generated US$361 million in its first seven months (**7**), and Yescarta reached $1.5 billion in annual sales by 2023 (**8**).

That clinical and commercial validation coincided with favorable investment conditions. Low interest rates, ample liquidity, and strong investor appetite for innovative therapeutics drove venture funding from about $13 billion annually in 2018 and 2019 to about $26 billion in 2021 and 2022 (**9**). Initial public offering (IPO) activity mirrored that trajectory, with biotechnology public offerings

reaching record levels in 2021 — over 100 biotechnology companies priced initial offerings and raised nearly $15 billion — before collapsing to just 22 companies in 2022 (**10**). Commercial successes, combined with available capital, encouraged widespread expectations that subsequent CGTs would replicate such performance.

Figure 2: Estimated workflow to meet clinical-trial demand; AAV = adenoassociated virus, CAR-T = chimeric antigen receptor T cell, LV = lentivirus



The COVID-19 pandemic fundamentally disrupted that trajectory through economic volatility, supply-chain disruptions, and shifting healthcare priorities as governments redirected investments toward COVID-19 vaccines and therapeutics. Healthcare-access restrictions reduced patient enrollment in non–COVID-19 clinical trials, with more than 2,000 other trials explicitly stopped by January 2021 due to COVID-19 restrictions (**11**). Although overall clinical-trial activity demonstrated resilience by 2022 as the number of non–COVID-19 clinical trials increased 8% above 2019 baseline levels (**12**), the CGT sector experienced prolonged disruption. Gene-therapy trials declined from a peak of 97 in 2021 to 77 in 2022 (**13, 14**), reflecting sector-specific challenges that persisted beyond general pandemic effects.

Despite lowered demand for non–COVID-19 therapeutics, expansion for viral-vector manufacturing capacity continued based on prepandemic projections and sustained funding availability, driven by newly emergent CDMOs and expansion by established players. The mismatch between supply build-out and actual market demand has contributed to a global structural supply–demand imbalance that characterizes today's viral-vector manufacturing environment. The resulting overcapacity creates a challenging operating environment for CDMOs that continues to reshape industry dynamics and competitive positioning.

Methods: Our latest analysis uses a multisource methodology to assess viral-vector supply demand dynamics through 2031. Our approach integrates three analytical frameworks: bottom-up clinical demand modeling, top-down commercial forecasting, and primary research-based capacity assessment.

Analytical Framework and Data Sources: The analysis period spans 2016–2031, with 2024 serving as the baseline year for forward projections. Data integration combines secondary sources — including GlobalData, ClinicalTrials.gov, regulatory

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databases, company financial reports, and industry conference presentations — with primary research conducted through engagement with CDMO representatives, academic institutions, and innovator companies that develop CGT products.

Figure 3: Clinical-demand data processing

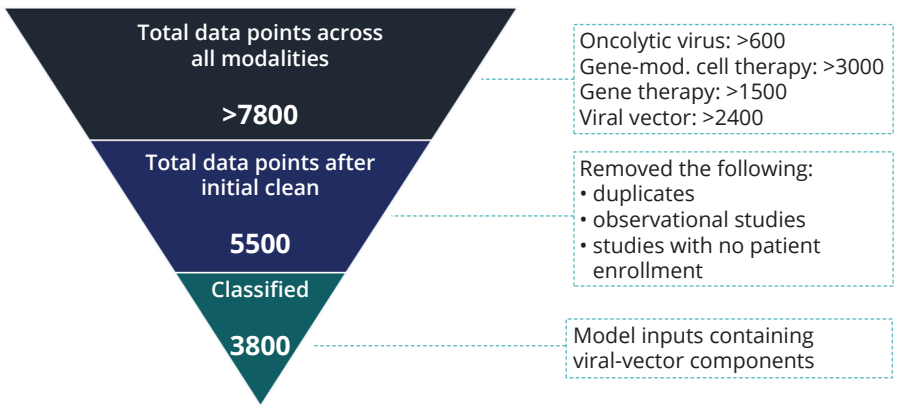
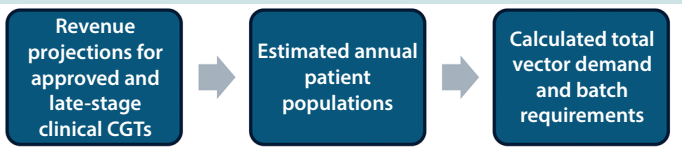


Figure 4: Estimated workflow to meet commercial demand; CGT = cell and gene therapy



Clinical-Demand Assessment: We've used a bottom-up modeling approach to project clinical demand to translate trial-level activity into manufacturing requirements (Figure 2). Online databases were queried systematically using standardized search terms, encompassing gene therapy, gene-modified cell therapy, and viral-vector applications. The extraction protocol captured trial start and completion dates, planned and actual enrollment figures, phase designations, and vector specifications across the analysis period (Figure 3).

Vector requirements were categorized systematically by vector type (AAVs, lentiviral vectors (LVVs), oncolytic viruses, and other) and therapeutic application. We included indication-specific subgroups based on modality, target tissue, and delivery route because such factors influence per-patient vector needs. Manufacturing batch requirements were calculated by applying vector-dosing assumptions to enrollment data, incorporating standard overages for quality-control (QC) testing and stability programs (40%) and vial-filling operations (20%). Batch calculations applied representative purified yields for each vector platform, derived from primary research with multiple CDMOs and validated against published manufacturing data.

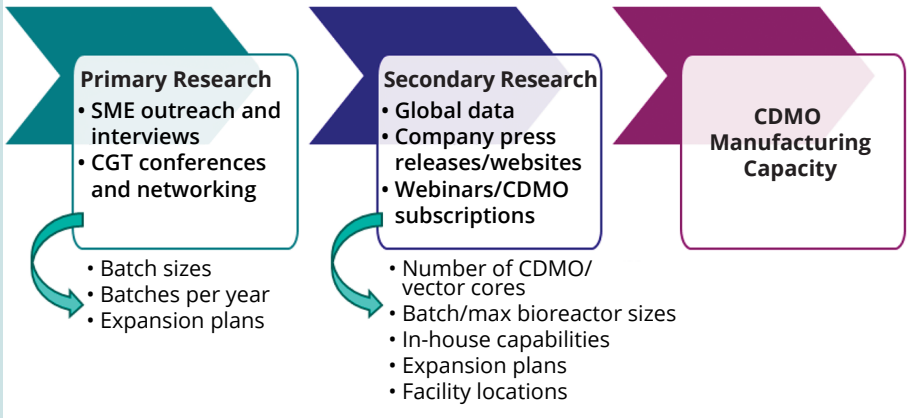
The clinical forecasting model projected trial-initiation rates and enrollment patterns based on historical trends. That approach captured the timing of manufacturing demand (typically occurring six months before trial initiation), scaling effects as programs advance through clinical phases, and attrition rates as programs discontinue or pivot during development.

Commercial-Demand Assessment: We evaluated commercial demand through a top-down analytical framework

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that translated market revenue projections into manufacturing requirements (Figure 4). Analyst revenue forecasts were collected from GlobalData and other secondary sources, focusing on approved products and late-stage clinical pipeline candidates. Annual patient numbers were calculated by dividing projected revenue by benchmarked per-patient prices of comparable drug products. Predicted patient populations were reviewed for reasonable market penetration assumptions.

Figure 5: Capacity workflow for contract development and manufacturing organizations (CDMOs); CGT = cell and gene therapy, SME = subject-matter expert



Vector-manufacturing requirements were calculated using the same indication-specific dosing framework established for clinical applications to ensure methodological consistency across market segments. Commercial batch requirements incorporated production-scaling factors that reflect the transition from clinical to commercial manufacturing, including yield optimization and process maturation gained through experience and the definition and refinement of process controls.

Manufacturing-Capacity Analysis: Manufacturing-capacity assessments combine primary research with systematic facility tracking to provide comprehensive supply-side intelligence (Figure 5). Primary research captured current operational capacity, usage rates, expansion plans, technology platforms, and yields of purified product. Academic vector core facilities similarly were assessed to understand their contributions to overall manufacturing capability.

Secondary research leveraged company disclosures, press releases, regulatory filings, and industry databases to assess global manufacturing capacity and track expansions. Our assessments included evaluation of in-house capacity at innovator companies and large pharmaceutical manufacturers. Capacity calculations incorporated bioreactor scales, number of production lines, throughput assumptions, and operational constraints that influence how actual production capability compares with theoretical capacity.

Modeling Assumptions: Key modeling assumptions reflected current industry practices and technological capabilities, with regular validation against primary research findings. Vector-yield

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assumptions incorporated platform-specific considerations, including productivity advantages across subtypes (e.g., AAV8/9 showing five-fold yield improvements) and production system differences (e.g., ≈10× higher productivity using baculovirus platforms) (Table 1).

Dosing assumptions were established through comprehensive analysis of clinical-trial protocols, with indication-specific categories reflecting the substantial variation in vector requirements across therapeutic applications (Table 2). In vivo vector dosages were categorized based on disease indication and route of delivery, including ocular, blood disorders, central nervous system (CNS), and muscle diseases. Ex vivo viral vector assumptions were based on manufacturing processes of approved CAR-T products, targeting 1.0×10^8 cells for modification, with multiplicity of infection (MoI) standardized at 5 (range of 1 to 10). Models were validated based on sensitivity analysis on key parameters, comparison with independently derived industry

Table 1: Vector-yield assumptions; CDMO = contract development and manufacturing organization, DSP = downstream processing, HEK = human embryonic kidney, IU = infectious unit, VG = vector genome, VP = viral particle

Vector	Purified Yield (200-L Suspension/iCellis 500 L)	Sources/Assumptions
Adenoassociated virus (AAV)	HEK293: 1.9×10^{15} VG Baculovirus: 1.2×10^{16} VG AAV8/9: 5× higher yield than base	Primary Research: >3 CDMOs
Lentivirus (LV)	1.0×10^{12} IU	Primary Research: >3 CDMOs
Oncolytic adenovirus (Ad)*	4.0×10^{14} VP	**1–5** 20–30% recovery from DSP
Oncolytic herpes simplex virus (HSV)*◊	2.0×10^{11} IU	**6–9** 20% recovery from DSP
Ad vaccine	4.1×10^{17} VP	**10**

* Oncolytic-vector yields can be affected by viral-genome modifications for replication specific to tumor cells.

◊ Identified references that give a better harvest yield from adherent Vero cells to update the model versus prior version

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Table 2: Representative adenoassociated virus (AAV) vector requirements; CNS = central nervous system, HEK = human embryonic kidney

	Ophthalmology (*N* = 5 Trials)	Genetic Disorders (*N* = 6 Trials)	Blood/ Hemophilia (*N* = 8 Trials)	Muscular Dystrophy (*N* = 4 Trials)	CNS (*N* = 8 Trials)	Cardiovascular (*N* = 2 Trials)
Phase 1/2 Study Patients	9	10	19	16	14	34
Phase 1/2 Vector Needed*	9×10^{12}	1.7×10^{14}	5.5×10^{16}	6.2×10^{16}	4.8×10^{15}	2.6×10^{15}
Average Vector/Patient	1.6×10^{12}	2.8×10^{13}	4.6×10^{15}	6.2×10^{15}	5.5×10^{14}	1.2×10^{14}
Patients/Batch	9	10	<1.0–3◊	<1.0–2◊	7	34
Batch-Size Assumptions: Average of HEK293 200 L / iCELLis 500 L and 200 L baculovirus						

* Based on the largest clinical dose with additional 60% material requirements to accommodate materials for quality control (QC) and/or stability testing (40%) and a finished overfill (20%)

◊ With AAV serotypes 8 and 9

estimates, and ongoing calibration against actual market developments.

Results: Our analysis and projections of viral-vector demand reveal distinct patterns across clinical and commercial applications, with significant differences in vector-type distribution and growth trajectories. Results have been translated to the necessary number of manufactured drug-substance batches to meet projected demand.

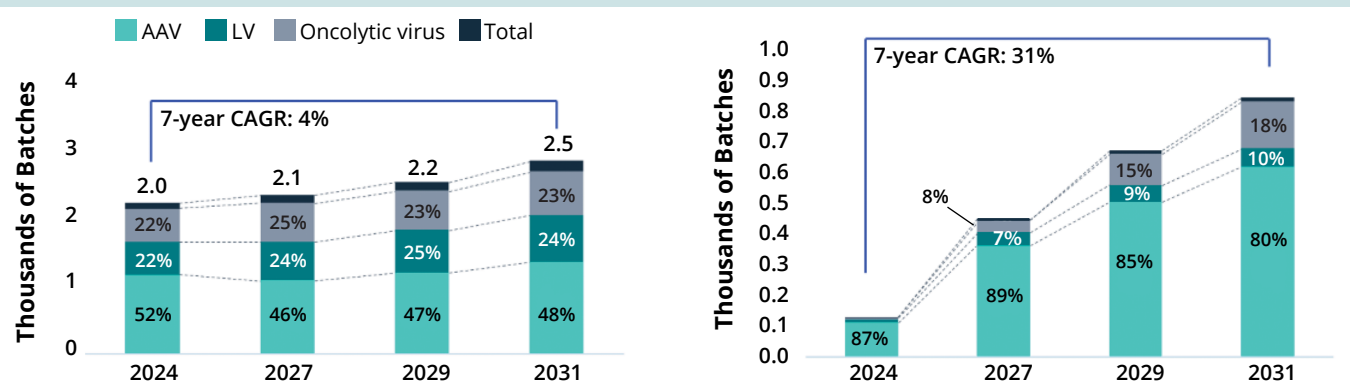
Vector demand for clinical-product development exhibits steady, albeit modest, growth at a 4% CAGR, with vector-type distribution remaining stable throughout the forecasted period (Figure 6, LEFT). AAVs make up about half of clinical batches, whereas LVs and oncolytic vectors each account for roughly one-quarter, showing minimal variation over time. Other vector types make up a small but consistent portion of demand.

Commercial applications demonstrate substantially different dynamics, growing at a 31% CAGR over the same period (Figure 6, RIGHT). AAV-vector demand dominates that segment, representing nearly 90% initially before declining to ≈80% by 2031 as oncolytic viruses capture an increasing share, with their portion growing from minimal levels to nearly 20%. LVs, which are used primarily to create gene-modified cell therapies, show modest but consistent gains from single digits to ≈10%, whereas other vectors remain minimal. That partition contrasts sharply with the more balanced clinical distribution.

Our combined demand analysis reveals divergent growth trajectories between the clinical and commercial segments of the CGT industry (Figure 7). Clinical growth remains consistent and gradual throughout the forecasted period, whereas commercial activity remains minimal through 2025 and should accelerate from 2026 onward.

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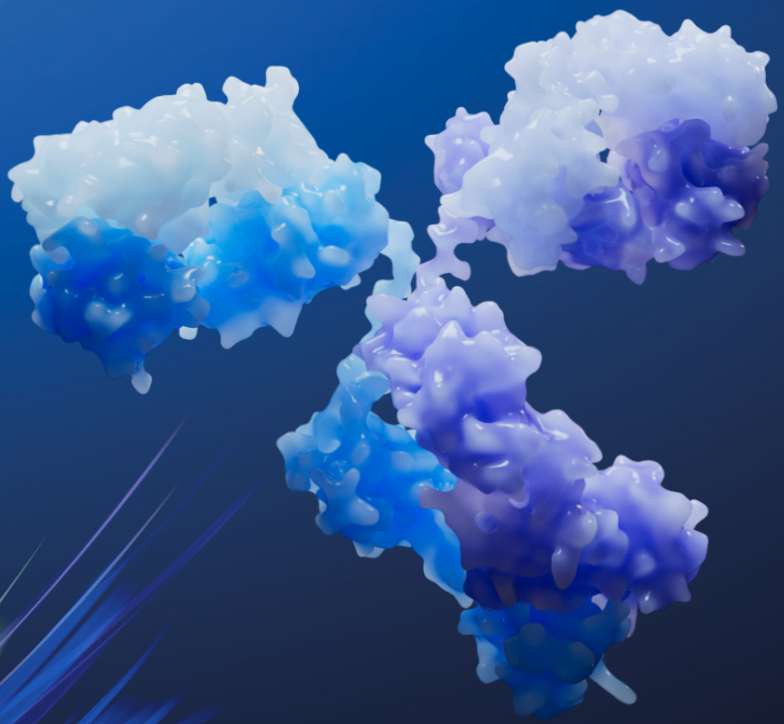
Figure 6: Clinical and commercial batch demands; AAV = adenoassociated virus, CAGR = compound annual growth rate, LV = lentivirus



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The capacity-forecasting model presents three scenarios reflecting different industry trajectories: continued expansion based on historical trends; moderated growth incorporating current market conditions and consolidation activities; and operational capacity adjusted for observed usage rates, with a 55% baseline assumption. That scenario approach addresses the uncertainty in capacity-planning decisions under current market conditions.

All capacity scenarios indicate oversupply across the forecasted period, with supply–demand balance approached only in the final forecast years as commercial demand accelerates. Our capacity projections align with emerging industry consolidation patterns and strategic repositioning already visible across the sector, remaining subject to potential disruption from biopharmaceutical innovations that fundamentally could alter vector requirements and production economics.

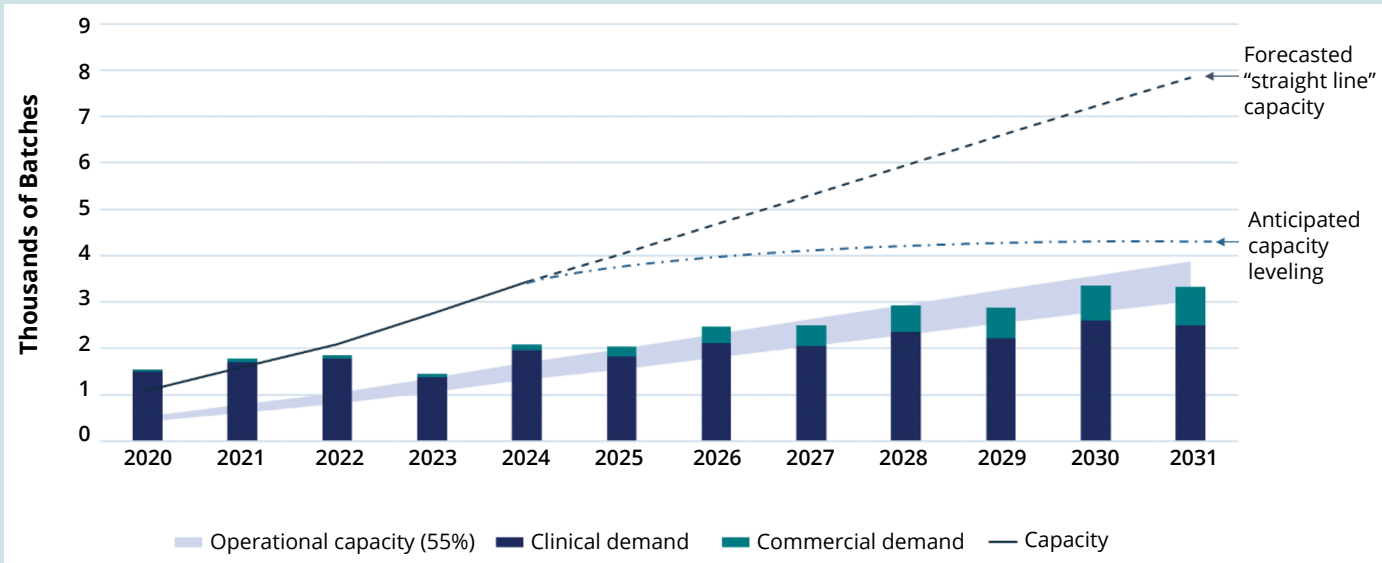
Model Assessment and Discussion

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Our analysis reveals a viral-vector manufacturing landscape characterized by global overcapacity, with available supply exceeding current demand across the forecasted period. Manufacturing capacity has expanded at rates that outpace actual market growth, creating challenging market dynamics for industry participants.

Industry Consolidation and Market Dynamics: Manufacturing infrastructure has expanded rapidly from ≈35 facilities compliant with current good manufacturing practice (CGMP) in 2018 to ≈80 such facilities by early 2024, as well as

Figure 7: Viral-vector batch demand versus capacity



significant expansion of established vendors. That growth has created supply–demand imbalances that increasingly favor market consolidation. As of early 2024, five major manufacturers controlled about one-third of total production capacity, although recent CDMO consolidations suggest that the concentration is shifting. Recent industry developments exemplify that trend, with contract manufacturers facing insufficient demand: Bristol Myers Squibb closed a viral-vector site in Chicago; AmplifyBio shut down after failing to find a buyer; and Thermo Fisher, Rentschler, National Resilience, and Charles River Laboratories all have reduced their workforces or closed facilities (**15**). Many newer CDMO entrants face considerable challenges securing sufficient contracts to support sustainable operations, potentially leading to facility deterioration or market exit.

Such capacity challenges reflect broad industry struggles extending beyond CDMOs to innovator companies. Major pharmaceutical companies have made strategic retreats from gene therapy. For example, Pfizer discontinued its approved hemophilia B treatment Beqvez (fidanacogene elaparvovec-dzkt) and left the gene-therapy field (**16**), whereas Vertex discontinued all AAV-vector research (**17**). bluebird bio, once valued at over $10 billion, was sold to private equity firms for $29 million (**18**), which represents a precipitous decline from its peak valuation.

The fundamental challenge is that positive projected demand for combined clinical and commercial growth of 8% CAGR cannot absorb the rate of capacity expansion that occurred in recent years. Even with commercial demand expected to grow at 31% CAGR, overall market expansion remains insufficient to take full advantage of existing manufacturing infrastructure.

Manufacturing and Process-Development Challenges: Manufacturing-efficiency improvements and cost-reduction strategies are becoming increasingly important for industry sustainability and profitability. The transition from adherent to suspension culture systems enables true scale-up rather than scale-out but presents technical challenges, including productivity losses and genetic-instability concerns.

Many CDMOs and developers have been working to establish vector-manufacturing platforms that constitute isolated human embryonic kidney (HEK) 293 cell lines with corresponding transient-transfection methods and downstream processing. Such platforms could reduce development timelines significantly and accelerate entry into phase 1 and 2 clinical trials. However, novel vector capsids and alternative envelope-entry proteins may not be compatible with established platforms and thus would require

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product-specific process steps for optimal vector recovery and quality. That could compromise the benefits of standardized manufacturing approaches.

Advances in vector engineering present additional complexity for demand forecasting. Innovations in capsid modifications to improve target cell transduction specificity may lower required vector doses per patient, potentially moderating demand growth despite expanding therapeutic applications. However, such developments must balance efficacy improvements against potential immunogenicity concerns that could limit repeat administrations.

Viral-vector products that target diseases with large patient populations (and thus have high vector demand) also influence manufacturing capacity. For such indications, innovators can transition to stable producing cell lines to overcome cost and scalability challenges associated with plasmid-based transient transfection. That approach could enable manufacturing at 2000-L scale and process-intensification strategies, which might affect vector yields and represent another variable for future capacity planning.

Process improvements and vector-engineering advances are converging to offer potential reductions in overall manufacturing demand. Process optimization can increase batch yields and reduce material waste, whereas enhanced vector efficiency requires lower doses per patient. Those complementary approaches can moderate demand growth, which could be offset by product development targeting diseases with large patient populations. Oncology-targeted products, such as CAR-engineered cells, continue to gain approval for treatment of earlier disease stages, thereby expanding patient populations and creating additional uncertainty for capacity planning decisions.

Realizing such benefits requires considerable investment in manufacturing technologies. Without advances in operational efficiency, automation, and process optimization, many facilities will struggle to maintain profitable operations.

Commercial, Regulatory, and Policy Considerations: Commercial adoption faces barriers beyond manufacturing-capacity constraints, including reimbursement challenges and patient willingness to accept treatment. Current reimbursement frameworks present significant hurdles for high-cost, single-administration therapies. Payers evaluate coverage for treatments costing hundreds of thousands to millions of dollars per patient. Although such therapies offer long-term cost benefits, coverage limitations restrict patient access and affect commercial-vector demand, creating a gap between regulatory approval and market uptake.

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Regulatory factors introduce additional variables into market dynamics. The regulatory environment continues evolving as agencies gain experience with novel therapeutic modalities, requiring ongoing industry adaptation. Recent leadership transitions at the FDA — such as departures of the directors of the Center for Biologics Evaluation and Research (CBER) and the Office of Therapeutic Products (OTP) — create operational uncertainties that affect product timelines, guidance-document priorities, and strategic decision-making during a period when regulatory frameworks for advanced therapies still are being refined.

Policy developments such as the BIOSECURE Act present supply-chain considerations for viral-vector manufacturing, potentially restricting partnerships with certain overseas manufacturers and forcing capacity reallocation to domestic or allied facilities. Evolving international regulatory harmonization efforts and differing approval standards in major markets require companies to navigate multiple regulatory environments with different and potentially divergent requirements for vector-based therapies.

Strategic Outlook

Excess manufacturing capacity is likely to reshape the viral-vector manufacturing sector, favoring organizations with demonstrated operational advantages and strategic positioning. Success will depend on manufacturers' ability to deliver consistent quality, competitive pricing, and flexible production capabilities that adapt to evolving therapeutic requirements. Some CDMOs will thrive while others struggle to compete. The long-term viability of viral-vector manufacturing requires production processes that can deliver therapies at economically sustainable costs while maintaining quality and scalability. Manufacturing efficiency and cost optimization will influence which therapeutic approaches achieve broad clinical adoption, making operational excellence an important differentiator in a capacity-abundant market.

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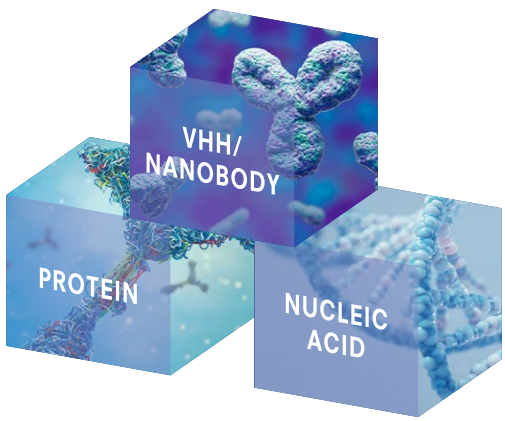
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