

Pharmaceuticals & Medical Products Practice

COVID-19 and cell and gene therapy: How to keep innovation on track

Cell and gene therapies promise life-changing treatments, but the pandemic has hit the sector hard. A survey reveals the extent of the disruption and suggests actions to help companies become more resilient.

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Cell and gene therapies (CGTs) are at the forefront of innovation to treat severe diseases, such as cancer, as well as rare diseases. Several such therapies are now on the market, including LUXTURNA, a treatment for an inherited retinal disease that causes blindness. That particular CGT represents an important medical milestone: it was the first curative gene therapy approved for use.

Many other CGTs are now in development. More than 750 trials of CGTs in almost 30,000 patients were underway as of June 2020, and CGT products account for some 12 percent of the pharmaceutical industry's clinical pipeline and at least 16 percent of its preclinical pipeline.¹ All that activity reflects the hope that CGTs will expand the still-limited treatment options available to many patients and transform the clinical paradigm. But the COVID-19 crisis has severely disrupted the sector.

While all biopharmaceutical companies have been affected by the COVID-19 pandemic, many CGT companies have been hit particularly hard because of their complex manufacturing and delivery model and their funding model. Both have proved to be fragile. A survey of executives at 20 European and US CGT companies reveals the extent of the disruption caused by the COVID-19 crisis and suggests how companies might respond—both to withstand the crisis and to lay the ground for success in a postpandemic world.² The actions companies take could prove critical for today's patients undergoing CGT and for those likely to benefit from the next wave of innovation that CGT companies are pursuing.

How the COVID-19 crisis is disrupting the cell- and gene-therapy industry

The manufacture and delivery of treatments, research and clinical development, and commercial operations are the three areas within the CGT industry that have been most disrupted by the COVID-19 crisis.

Treatment manufacture and delivery

The COVID-19 health crisis has been more severe in some regions than in others, which means that some CGT companies have emerged relatively unscathed. But in regions where the novel coronavirus (which causes COVID-19) has been prevalent, CGT companies have found themselves highly susceptible to disruptions because the supply chains that support the manufacture and delivery of CGTs are long, complex, and highly controlled (Exhibit 1).

That susceptibility is particularly true of cell therapy. Cell collection, the first step in the manufacturing process, has been a major point of disruption for companies. Many apheresis centers have stopped operating to limit the exposure of healthcare practitioners (HCPs) and cell donors to the novel coronavirus and because their personnel have been reassigned to help manage the health crisis. In addition, closed borders, reduced air traffic, and delayed flights have endangered the viability of the material collected, as it is both time and temperature sensitive.

Supply shortages have also caused problems. For example, a cell-therapy company experienced long delivery times for certain plastic components and then found itself short of clinical-trial material when a partner contract-manufacturing organization was forced to shut down. In some instances, companies have been able to work with governments and healthcare systems to make sure that cell donors remain safe and to circumvent travel bans by helping to secure capacity on cargo flights instead of passenger flights or providing waivers for travel restrictions. Notwithstanding, the survey makes clear the limited impact of such measures. One-third of cell-therapy companies report manufacturing delays or a complete halt to operations, while one in five report disruptions in the procurement of supplies (Exhibit 2).

The manufacture of gene therapies has been less affected. Some 60 percent of survey respondents report no disruption to their operations, reflecting a less complex manufacturing and delivery model.

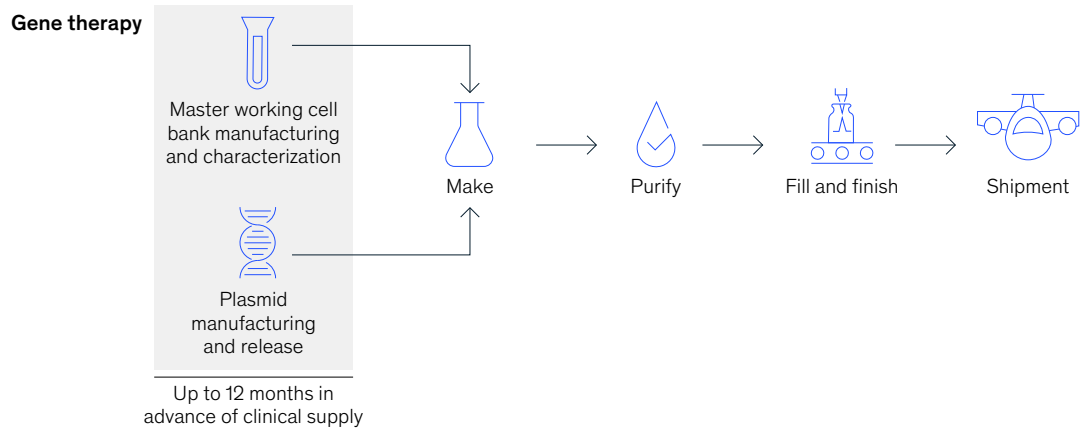
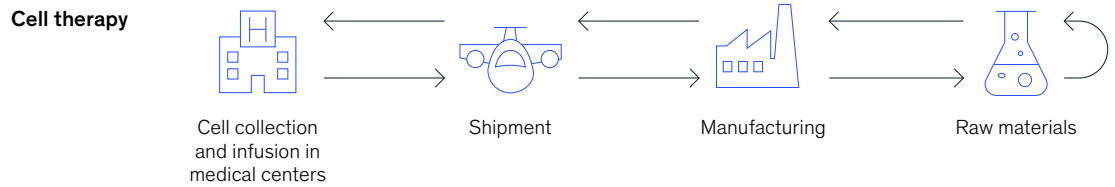
¹ Toby AuWerter, Jeff Smith, and Lydia The, "Biopharma portfolio strategy in the era of cell and gene therapy," April 2020, McKinsey.com.

² Executives were surveyed during virtual roundtables on May 8, 2020.

Exhibit 1

The supply chains that support the manufacture and delivery of treatments are long, complex, and highly controlled.

Cell-therapy and gene-therapy supply chains



The main problem encountered has been the timely delivery of therapies to clinical sites and patients.

The administration of both types of therapies has also proved problematic. Hospitals concerned about the transmission of the novel coronavirus, especially to more vulnerable patients, have canceled or delayed appointments. And patients themselves have been unable to visit treatment centers because of travel bans. In addition, some treatments need to be administered in intensive-care units that have been reserved for COVID-19-infected patients.

Research and clinical development

Across the CGT sector, research programs and preclinical activities have been disrupted as companies have reduced the number of people

working on site to keep them safe and conform to government advice. Many research sites have been operating at below 50 percent of normal capacity. For example, a CGT company has had 85 percent of its employees working from home for several weeks. Another's staff shortages have delayed its assay development and hence its submission of a Biologics License Application to the US Food and Drug Administration.³ Research and preclinical development have also been affected by the high demand for COVID-19-related laboratory consumables, such as personal protective equipment and reagents, causing supply shortages.

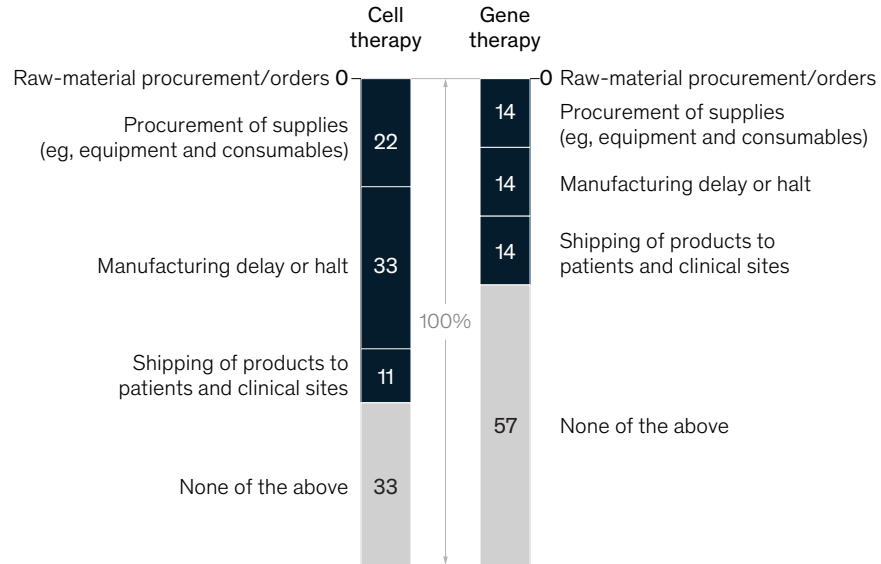
But clinical development is the area that has suffered most. More than half of the CGT companies surveyed report difficulties in recruiting patients or

³ A Biologics License Application is submitted to the US Food and Drug Administration to obtain permission for the distribution of a biologic product.

Exhibit 2

One-third of cell-therapy companies reported manufacturing delays or a complete halt to operations, while one in five reported disruptions in the procurement of supplies.

Areas of disruption, % of respondents¹



¹Figures may not sum to 100%, because of rounding.
Source: COVID-19-pandemic impact on the cell- and gene-therapy industry, virtual roundtable, May 8, 2020

having to suspend trial enrollment to minimize the risk of COVID-19 exposure for participants. That has meant delays in activating new sites and the postponement of new trials. It is worth noting that the level of disruption for CGT trials appears to be lower than that experienced more broadly in the pharmaceutical industry, possibly reflecting the facts that CGTs address serious and rare conditions and that clinics and patients alike are determined to continue those trials if at all possible.⁴ Nevertheless, difficult decisions have had to be made. For example, weighing the risks, a CGT company decided to halt trials in pediatric diseases but continue with those in oncology.⁵

Patient assessment has also proved challenging. Some 55 percent of surveyed companies say they

had missed follow-up assessments of patients already in trials. Travel restrictions, patient concerns about being exposed to the novel coronavirus or actually catching it, and the withdrawal of all but essential services from some healthcare sites have been contributing factors.

Such disruptions go beyond delaying development. They could threaten the viability of some CGT companies. That is because many are small biotech enterprises still at the precommercial stage and therefore reliant on external funding. In the absence of product sales, funders—venture capitalists, shareholders, governments, and pharmaceutical corporations—make investment decisions based on pipeline progress, key-data readouts, and specific research milestones. Yet almost two-thirds of the

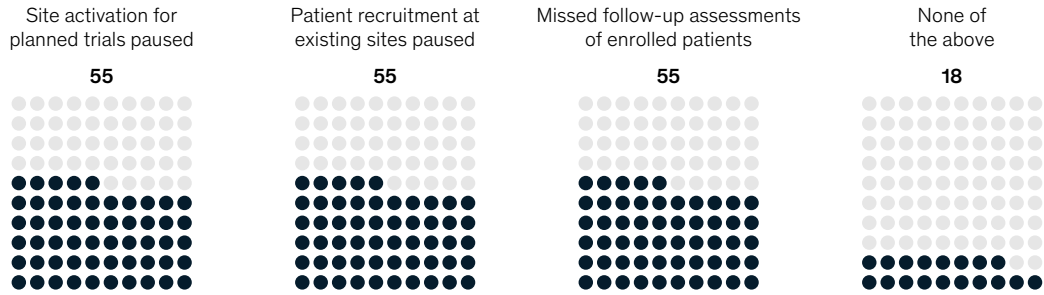
⁴ Gaurav Agrawal, Brandon Parry, Brindan Suresh, and Ann Westra, “COVID-19 implications for life sciences R&D: Recovery and the next normal,” May 2020, McKinsey.com.

⁵ “Moderna provides update on the impact of COVID-19 on business operations and clinical program development,” Moderna, March 29, 2020, modernatx.gcs-web.com.

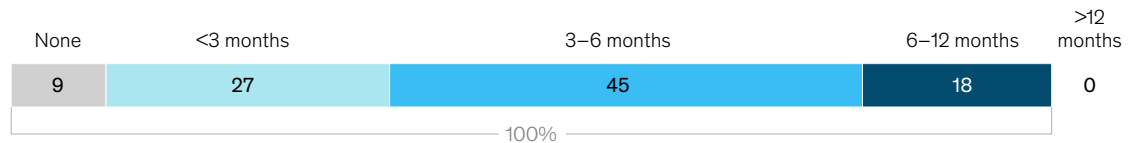
Exhibit 3

A survey of disruptions in R&D activities revealed many problems: 45 percent of respondents expected delays of three to six months on average for development programs.

Areas of disruption in clinical development, % of respondents



Average delay expected in development programs, % of respondents¹



¹Figures may not sum to 100%, because of rounding.
Source: COVID-19-pandemic impact on the cell- and gene-therapy industry, virtual roundtable, May 8, 2020

European and US CGT companies in the survey expect their development programs to be delayed by more than three months, while one in five expect a delay of six months or longer (Exhibit 3).

As a result of those delays, some CGT companies are struggling to raise more funding. Of the small to midcap public CGT companies in the United States, 43 percent are likely to need new funds in the next 12 to 24 months—funds that could become more difficult to raise, given delays to clinical-development programs and data generation. Moreover, of the assets or companies that need funding in the next 18 months, 44 percent are in Phase II trials and require a significant level of new funding to progress further (Exhibit 4).⁶

Commercial operations and access

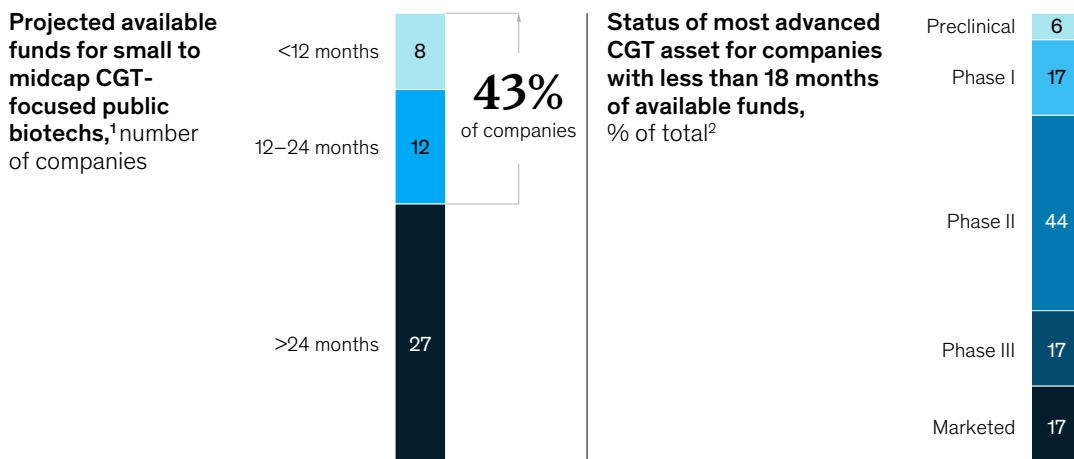
Disruptions to the commercial operations of CGT companies have been widespread. Of the European and US companies in the survey, 50 percent report a reduction in engagement with HCPs, clinical sites, and patients (Exhibit 5).

The pandemic brought to a halt the face-to-face interactions that CGT companies were used to having with HCPs. Many companies moved quickly to use digital channels instead, but the frequency of engagement fell, and the focus was often on coordinating the delivery of care rather than generating new interest in the CGTs. Likewise, the lack of contact has meant less engagement with investigators, a critical source of input into

⁶ Analysis of data gathered from cell- and gene-therapy companies' websites; ClinicalTrials.gov; "COVID-19: Implications for business," full briefing materials, April 13, 2020, McKinsey.com; EvaluatePharma, Evaluate, April 2020, evaluate.com; and Corporate Performance Analytics by McKinsey.

Exhibit 4

Many publicly listed cell- and gene-therapy companies will need more funds before the economy recovers from COVID-19.



¹As of Dec 31, 2019. Analysis includes all US public biotech companies with market capitalization of between \$300 million and \$10 billion at end of FY 2019, and whose CGTs account for a major part of their valuations. Ten of a total of 57 companies are excluded because of limited data. Assumes burn rate remains constant; runway calculated as 2019 year-end cash and short-term investments/2019 net income * -1.
²Figures may not sum to 100%, because of rounding.
 Source: Annual reports; McKinsey Corporate Performance Analytics Tool; EvaluatePharma, Evaluate, April 2020; company websites; McKinsey COVID-19 briefing materials, April 13, 2020; Clinicaltrials.gov

treatment-launch preparation and the translation and dissemination of trial data into clinical care.

Engagement with patients has also suffered. While CGT companies have looked to support patients during the pandemic through patient organizations, patient access to treatment has fallen. Many hospitals and clinics have been unable to initiate new, complex treatments, such as CGT. In addition, financial constraints, accentuated by the COVID-19 crisis, may have limited some patients' access to the costly therapies.

Access to CGTs has been further delayed because launch plans have had to be rethought. One-third of the companies surveyed say their launch plans have been modified or postponed. Disruptions to clinical development, delays in the regulatory process, and an inability to commence treatment are among the reasons cited.

Engagement with payers has become more difficult, too, potentially affecting access and reimbursement. And companies are aware that the capacity of

regulators themselves has been constrained. Chemistry, manufacturing, and controls inspections can be affected by travel bans, for example, which could hit a CGT company's development and approval time lines.

How to navigate crisis recovery

CGT companies have taken a range of measures to manage the immediate effects of the COVID-19 crisis. However, once the spread of COVID-19 slows and healthcare systems return to more normal operations, CGT companies will have to work hard to get development programs back on track and ensure that their manufacturing and delivery processes are more robust. They will also have to work more closely with physicians and patients to safeguard the future commercial success of their therapies.

Bring development programs back on track

A priority for any CGT company must be to restore the smooth running of clinical-development programs. The specific actions taken will probably

Exhibit 5

Disruptions to commercial operations have been widespread: 50 percent of companies report reduced engagement with healthcare professionals, clinical sites, and patients.

Reduced engagement with sites, healthcare professionals, and/or patients	Launch plans modified/ launch date postponed	None of the above
50	33	17
Significant resources reallocated to different or new commercial activities (eg, digital) 0	Revised sales projections 0	Decrease in sales (if relevant) 0
100%		

Source: COVID-19–pandemic impact on the cell- and gene-therapy industry, virtual roundtable, May 8, 2020

depend on technology, disease area, and geography. Every company will benefit, however, from a plan that lays out the trials that can be started or reopened, when, and where, based on epidemiological data, geographic restrictions, and an assessment of the capacity of local health systems and involved trial sites. Having the right data will give companies the agility required to navigate what is likely to be a fast-changing environment.

In addition, CGT companies might consider the following measures:

- **Adjust trial protocols.** Consider whether trial protocols can be adjusted, with a view to decreasing the frequency of patient visits, medical procedures, and data-collection points. Rather than asking patients to visit clinics, use home visits or digital tools for remote monitoring. That should encourage patient recruitment and adherence to follow-up schedules, as trials are still concentrated in a few specialized sites, often requiring patients to travel long distances to participate. Telemedicine has become commonplace during the pandemic—a clinical-research site has reported being able to conduct 60 percent of its patient appointments remotely.

- **Find ways to bridge data gaps.** Analysis and modeling of available data may help provide some guidance on bridging data gaps. And

electronic medical records can be used to verify and enrich source data remotely.

- **Stay close to regulators.** Excellent connections with regulators are helpful for discussing and mitigating regulatory issues, such as data gaps and protocol deviations, that may have arisen during the COVID-19 crisis. And good relationships forged now could help CGT companies benefit from the increased flexibility and openness that regulators have demonstrated in their response to COVID-19—a stance that may well extend to the future regulation of CGT.

Make the manufacturing and delivery model more resilient

In the absence of an effective vaccine against COVID-19, the threat of disruptions to the manufacture and delivery of CGTs remains. The current pandemic is far from over, and new outbreaks are a possibility. Finding ways to ensure business continuity is therefore crucial. Half of the CGT companies surveyed say they have plans to improve supply-chain resilience and address bottlenecks in their current processes.

Those measures include increased use of digital tools and analytics to provide better insight into the supply chain, reduced reliance on single suppliers, and more manufacturing capacity, and

they are applicable to any pharmaceutical company. But there are several other measures that are particularly relevant to CGT companies:

- **Secure the supply of constrained value-chain steps.** Manufacturing capacity for viral vectors was constrained before the COVID-19 crisis but could become tighter still as efforts progress to develop and manufacture what could be billions of doses of a COVID-19 vaccine. Many of the raw materials and consumables used to manufacture viral-vector-based vaccines are the same as those used to manufacture gene therapies. While more viral-vector manufacturing capacity is the long-term answer, CGT companies might consider strategic partnerships with key suppliers of critical raw materials and viral vectors, or identify and validate two to three potential suppliers early in the development process, rather than relying on just one.
- **Prepare for remote working.** For the foreseeable future, travel restrictions and physical-distancing guidelines could hamper key work processes, prompting the adoption of digital tools to help manage them seamlessly and with minimal supervision. For example, digitization of all documentation allows for remote access and a reduced need for on-site personnel. Companies that are beginning to scale up manufacturing as their businesses grow may also wish to reconsider the criteria for selecting manufacturing partners. Reliability may factor more highly in an age when physical visits and checks are restricted, perhaps countering cost considerations. So, too, could a partner's preparedness for remote site inspections and virtual audits. Regulatory authorities, such as the US Food and Drug Administration, have already started to implement related measures, which means manufacturers need the right IT infrastructures and processes in place to facilitate them.

- **Consider a model redesign.** Ultimately, more drastic measures may be required, as the COVID-19 crisis has exacerbated the fragility of the business model of CGT companies. The cost of therapy has already sparked debate as to whether commercial success will depend on new payment models to help payers absorb the costs while offsetting the risks of what remain novel treatments.⁷ But the pandemic has also shown how vulnerable manufacturing and delivery are to external disruptions because of the complexity of the supply-chain and production processes. A more resilient manufacturing and delivery model might require a completely different approach, possibly bringing the manufacturing and delivery of therapies to a single site—the point of care. While the current crisis has put the CGT manufacturing and delivery model under pressure, novel solutions, such as unprecedentedly rapid tech transfer, have been designed for COVID-19 vaccines, and CGT companies can adopt and implement them as their new standards.

Move closer to patients and physicians

CGT companies will need to work hard to reengage with HCPs, and digital tools and capabilities will be the cornerstones of those efforts. A survey found that 43 percent of physicians said they would have far fewer face-to-face meetings with pharmaceutical-company reps after the COVID-19 crisis.⁸ CGT companies are already responding. One-third of those in our survey say their field teams are now working differently, spending less time on the road. Many are also accelerating the rollout of tools for virtual engagement and looking at new ways to disseminate educational material.

In addition, companies will need to double down on efforts to support patients seeking access to CGT or undergoing treatment, bearing in mind that the future in that area is digital, too: digital tools can ease patient burdens and build reliance. Integrated support across the entire patient journey is the goal,

⁷ Toby AuWerter, Jeff Smith, Josh Sternberg, and Lydia The, "Unlocking market access for gene therapies in the United States," August 2019, McKinsey.com.

⁸ Sermo COVID-19 Healthcare Practitioner Survey, April 2020.

For the time being, most CGT companies don't foresee a major shift in their portfolio strategies. But there is little doubt some may need to reassess the value of individual assets if funding becomes tight.

providing help in determining eligibility for treatment, securing treatment access, initiating therapy, and managing and monitoring disease progression and therapy. Solutions could include financial-planning tools (to provide options for addressing funding shortfalls and accurate, real-time pictures of a patient's out-of-pocket costs) and innovative services that help patients get started on their treatments—for example, 24-hour availability to deliver an at-home starter package and adherence tools, such as digitally enabled physical tracking from day one.

The CGT industry is in uncharted territory, facing its first-ever crisis. Many companies have been forced to change the ways they operate and to introduce innovative and more efficient processes. In some respects, the COVID-19 crisis has accelerated changes that were afoot, such as the broader use of telemedicine and the application of advanced analytics. The pandemic has also supercharged innovation. Concerted efforts to develop RNA-based COVID-19 vaccines could demonstrate proof of concept of RNA platforms within months, accelerating progress in some gene therapies.

For the time being, most CGT companies do not foresee a major shift in their portfolio strategies. But there is little doubt that some may need to reassess the value of individual assets if funding becomes tight, investing less in some areas and accelerating the development of others. And now, more than ever before, CGT companies will need to demonstrate that the costs of their treatments are offset by the outcomes and long-term, measurable patient benefits.

While the pandemic has highlighted the importance of R&D in the biopharmaceutical industry and sparked public debate about how it should be funded, the fact remains that funding for healthcare systems will probably come under pressure as lockdown-driven recessions begin to bite. Emerging and costly technologies could suffer as result, and the likelihood of price scrutiny by regulators is high. CGT companies still have the potential to be successful and deliver life-changing treatments to large numbers of patients. Companies that act quickly will be the ones that turn the current unprecedented challenge into a unique opportunity to make themselves more efficient and more resilient to whatever the future might hold.

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