FROST & SULLIVAN

BEST PRACTICES AWARDS

ALMAC

2020 GLOBAL JUST-IN-TIME MANUFACTURING SOLUTION FOR CLINICAL TRIAL SUPPLY COMPANY OF THE YEAR AWARD

Background and Company Performance

Industry Challenges

Chronic conditions are becoming more prevalent, along with the rapidly aging population. At the same time, the continuous evolution towards value-based care is driving precision medicine (PM)—delivering the right treatment to the right patient at the right time—as a foremost healthcare strategy going forward. Likewise, Frost & Sullivan analysts monitor how the pharmaceutical (pharma) industry is implementing patient-specific drug development approaches, moving away from the blockbuster 'one-size-fits-all' drug model, and embracing more tailored therapeutics where biologics are taking center stage.

Groundbreaking therapeutics over the last decade in cancer, mainly immuno-oncology (IO), autoimmune diseases, and rare illnesses, propelled the current development explosion, with biologics outpacing the overall pharmaceutical (pharma) spending—at a compound annual growth rate (CAGR) of 9.2%, versus small molecules' 2.2% from 2020 to 2025.[1] Cell and gene therapy, in particular, is a sector with high investment, growing at a CAGR of 22% from 2017 to 2022. Frost & Sullivan estimates the global biologics market to reach $489 billion by 2025.[2]

Many drug sponsors progressively outsource services central to drug discovery and development to improve their processes, generate efficiencies, and enhance decision-making. Frost & Sullivan anticipates an increase in outsourcing both clinical and commercial stage manufacturing over the next five years. Maturing biologics pipelines and biosimilar prospects will lead to excess demand in 2020. The global biologics contract development and manufacturing market will expand from about $12 billion in 2019 to over $17 billion in 2022, growing at a CAGR of nearly 13%.[3]

Over the past two decades, contract development and manufacturing organizations (CDMOs) became integral to drug sponsors' cost-containment strategies and a key stakeholder on a drug's ultimate success. Still, significant gaps exist at each stage in the pharma value chain to meet the evolving development demands cost-effectively. Clinical testing, the most time-consuming and resource-intensive phase, notably remains a critical hurdle despite advances in science and technology. Today, fewer than 12% of drugs entering the clinical stages obtain Federal Drug Administration (FDA) approval, and estimated failed clinical trial's costs range from $800 million to $1.4 billion.[4]

Growing Global Demand for Biologics Drives Patient-centric Clinical Trials

PM is fueling clinical trial globalization, multiplying protocol and regulatory complexities and costs, and, along increasingly complex development processes and technologies, impacting clinical trial efficiencies. Growing immunotherapies, alongside a strong potential for personalized cell and gene therapies, are further shifting the market paradigm towards low-

[1] *Frost & Sullivan proprietary information, April 30, 2020*
[2] *Ibid*
[3] *Global Biologics Contract Development and Manufacturing Organization (CDMO) Market, Forecast to 2022, (Frost & Sullivan, September 2018)*
[4] *http://phrma-docs.phrma.org/files/dmfile/ChartPack2018_PDF_6.28.18_final.pdf*

volume high-value biologics manufacturing, adding yet another intricacy level.

This hyper-complex, dynamic landscape poses severe challenges to supporting cost-effective, patient-centric manufacturing efficiencies.

Besides having a shorter shelf life and expiration dates, biologics are much more sensitive to handling and storage conditions compared to small-molecule counterparts. These drug products often require advanced cold chain solutions and tight logistical windows as variations can affect drug safety, potency, and purity, bearing both substantial clinical and economic significance. Drug sponsors need to reconcile costly and more sophisticated patient-centric, multi-vendor, multi-regional clinical trials with lean, flexible, and smaller manufacturing operations to mitigate the development risks and increased costs associated with highly variable patient enrolment practices.

Frost & Sullivan notes that biologics come with a hefty price tag. Leading contract development and manufacturing organizations (CDMOs) are expanding their service portfolio to align their products, expertise, and resources with up-and-coming biologics. For instance, incorporating end-to-end cold chain management with temperature-controlled packaging caters to the burgeoning cell and gene therapy sector. Vendors are also decoupling primary and secondary packaging services to provide more flexibility. CDMOs, however, must go further to reduce wasted resources, avoid costly development delays and clinical trial cancellations, and limit protocol deviations effectively.

Compliant and patient-led, demand-driven biopharma supply chains are the next frontier. Frost & Sullivan recognizes 'just-in-time' manufacturing (JTM) as a next-generation approach to enhance sponsors' profitability and, more importantly, ensure high-quality drug availability to patients.[5]

Visionary Innovation & Performance and Customer Impact

Headquartered in Craigavon, Northern Ireland, United Kingdom (UK), privately-held Almac Group (Almac) is an established global full-service CDMO for the pharmaceutical industry.

Almac offers comprehensive, integrated systems and tailored solutions spanning the product development life cycle, for both small and large molecules, through five distinct but interconnected business units: Diagnostic Services, Sciences, Pharma Services, Clinical Services, and Clinical Technologies.

Through continuous investments in technology, capabilities, and people, the company steadily expands its offerings to meet both its sponsors' dynamic needs and regulators' evolving requirements. Almac reports revenues of £548 million in 2018 and an 8% increase in its global force from 2017 to 2018.[6]

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[5] *Global Biologics Contract Development and Manufacturing Organization (CDMO) Market, Forecast to 2022, (Frost & Sullivan, September 2018)*

[6] *https://www.almacgroup.com/news/almac-group-reports-further-growth-during-period-of-significant-global-expansion/*

Almac: Mission-driven, Pioneering Leadership

Over the last 50 years, Almac harnessed industry-leading technologies, world-class expertise, and service excellence across its business units with a sharp, sustained focus—"Partnering to Advance Human Health."

Under its stated purpose, the company capitalizes on novel, robust methodologies to develop customer-led, patient-centric solutions to drive innovation. With cost-efficiencies and speed-to-market as crucial success factors, Almac maximizes opportunities for its partners through customized, streamlined end-to-end services underpinned by high quality, flexible, and cost-efficient project management options.

Customer-led, Patient-centric Innovation

Standard batch manufacturing often results in wasted high-value Investigational Medicinal Products (IMP)—mainly technologically complex, sophisticated biologics and smaller, yet global, clinical studies. These large molecules, with intrinsic instability and in limited supply, compel frequent re-testing for expiration updates, driving up both costs and inefficiencies.

In essence, nearly all IMPs and, thus, also comparators are injectable with both inner components, e.g., vials and syringes, and packaging materials. All components require country-specific labels, in the local language, relaying critical information such as assembly and dosing instructions, storage conditions, and drug expiry. Batch manufacturing operations are a futile endeavor in a fluid, patient-centric clinical trial landscape, whether replaced due to expiry dates, outdated dosing, or destroyed owing to unrealized demand. Conventional manufacturing practices add to time and cost burdens to already time-consuming and expensive processes, and, more importantly, can delay patients' access to potentially life-saving treatments.

"Time is precious for patients. We [Almac] do not want patients' to wind up without access to critical medications for their life."

— Mark Rohlfing, Vice President Operations , Almac Group

"We know the patient is our end game so, patients are at the forefront of everything we do—our key driver."

—Jennifer Erwin, Senior Marketing Associate, Almac Group

Almac builds on existing cold chain management and just-in-time solutions, e.g., labeling, to streamline standard manufacturing. In 2018, the Clinical Services group supported Pfizer on Phase Ib clinical trials for a novel Duchenne muscular dystrophy (DMD) gene therapy in pediatric patients. Almac set forth a LEAN clinical trial packaging and labeling process to uphold Pfizer's mission-critical dosing of a child diagnosed with DMD in 12 days versus at least 4 weeks using batch manufacturing.[7]

This industry-leading LEAN packaging process became the blueprint for the company's pioneering JTM solution, developed over several years as a systematic response to drug sponsors' increasing challenges with their growing biologics pipelines.

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[7] *https://www.manufacturingchemist.com/news/article_page/Lean_packaging_by_Almac_supports_Pfizers_mission_to_dose_patient_with_life-enhancing_gene_therapy/161763*

In mid-June 2019, the Clinical Technologies group launched Almac Adapt™, further disrupting the conventional batch manufacturing approach.

Almac ADAPT™: The Future is Here

"JTM is essential in making personalized clinical trials successful and easier to manage. One of the biggest motivators for an on-demand or a 'pull strategy' is asking your supply chain to pull the product through based on an actual need rather than try to push the product into the supply chain where the demand does not exist."

—Natalie Balanovsky, JIT Manufacturing Solutions Manager, Almac Group

Almac ADAPT™ is a full, late-stage clinical kit customization solution. It supports PM clinical trial design, making patient-specific kits on-demand when the site or patient need arises; thus, bolstering clinical trial manufacturing cost-efficiencies. Key advantages to conventional batch manufacturing approaches include on-time patient kit delivery, reduced study timelines, limited high-value product wastage and shortages, and a flexible and agile supply chain management process adjusting to mid-study protocol changes.

With the solution as part of a larger umbrella, Almac uses a consultative approach for engaging drug sponsors. The company first ascertains whether JTM is the ideal solution for their specific problem and, if applicable, sets the protocol parameters, i.e., the pre-production phase. Almac uniquely leverages its full supply chain and end-to-end support, e.g., global logistical and temperature services, to further streamline processes.

Unlike the few other competitors in the space, Frost & Sullivan analysts recognize the way that the company's end-to-end JTM solution ensures the product's viability alongside the most critical up-to-date information, from the moment it arrives at Almac, all the way through to the end of the supply chain, the end-user—typically the clinical site and the patient.

Beyond a Lean Manufacturing Style: A Systematic Approach

"Almac ADAPT™ is not only a manufacturing style. It is a systematic process we developed while working with Pfizer. Leveraging our ERP system, COSMOS can manage these supplies effectively, accurately and efficiently removing the need for manual intervention."

—Natalie Balanovsky, JIT Manufacturing Solutions Manager, Almac Group

Pre-production

A dedicated Almac Adapt™ team works closely with drug sponsors to establish the pre-production parameters. The collaborative effort results in creating the project's master documentation, aligned with the sponsors' trial constructs, timelines, anticipated patient enrollment, and participating clinical sites.

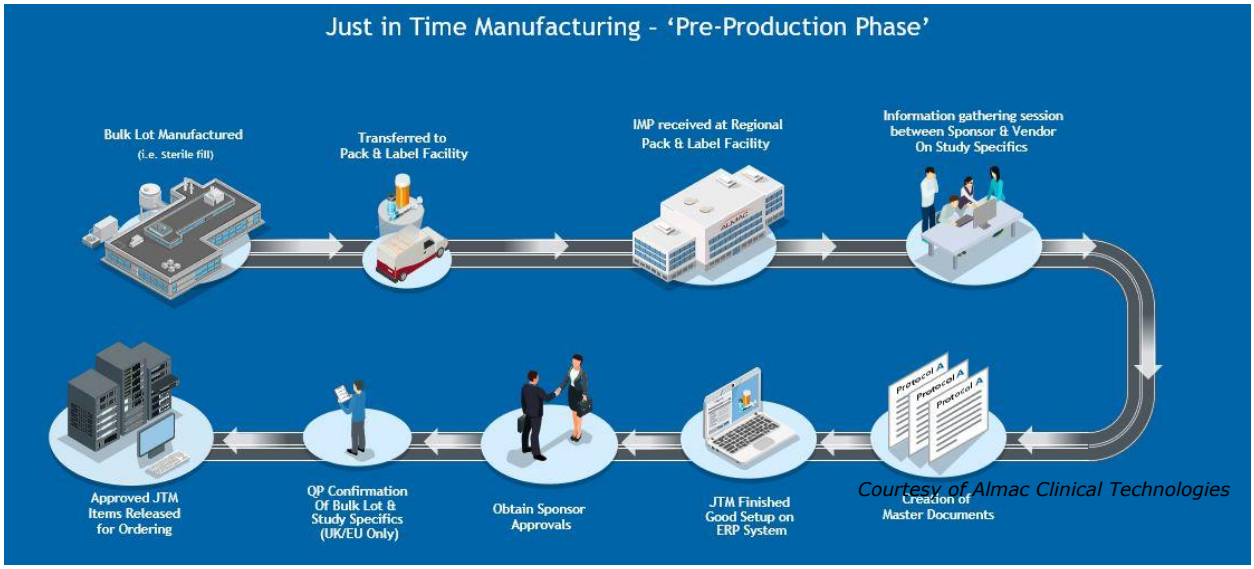
These pre-production documents define, identify, and direct the operational packaging and labeling needs, ahead of the first enrolled patient, serving as a reference guide. The pre-production master set contains all the information necessary for on-demand product distribution, e.g., country-specific labels, clinical kit assembly instructions, handling and storage conditions, and unique regulatory guidelines for the region.

Almac Adapt™ relies heavily on Almac's advanced Clinical Services Ordering and Supply Management Operating System (COSMOS) to optimize the entire clinical supply value chain. Its centralized enterprise resource planning and material resource planning (ERP/MRP) solution strengthens the company's JTM value proposition. The automated, tailored planning and scheduling, manufacturing framework removes the human error risk factor from the documentation workflows.

While this process is ongoing, the drug manufacturer sends its bulk material to the company, whether in solid dose or vial and syringes, completing manufacturing and technology readiness.

With the pre-production phase firmly in place, the on-demand drug order forms kick off the process.

Amac Adapt™: Pre-production Phase



Courtesy of Almac Clinical Technologies

Production and Distribution

"We must be as smart as possible with our valuable drug supply for the good of the patient. As such, we must be prepared to quickly adapt that supply to change we know will come. Rigid, fixed clinical trails just do not exist, no matter how well we plan."

—Mark Rohlfing, VP Operations, Almac Group

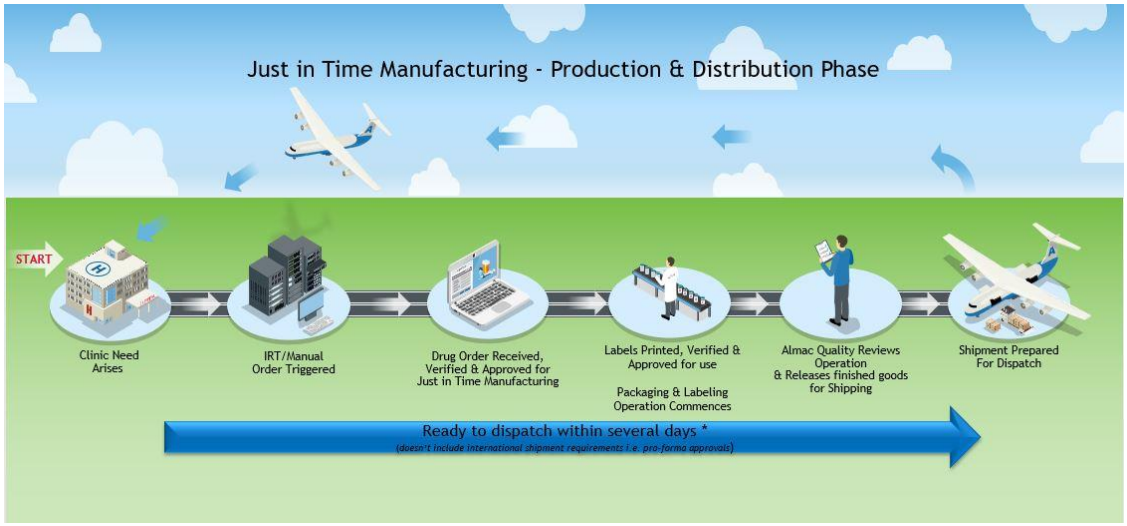
Almac waits until receiving a drug order from a site or depot before packaging, labeling, and assembling the clinical kit. As it accepts the distribution order forms, the company validates the information against the pre-production master document set in COSMOS, adjusting the system to protocol changes, if needed, throughout the operational execution and final distribution.

By establishing and approving quality process far in advance—vetted by both Almac's and the sponsor's quality teams—rather than creating documentation at the last minute, the company

provides unrivaled flexibility and speed. Almac Adapt™ allows for a rapid turnaround, i.e., within a matter of days, to support an actual patient demand and request for medication.

Additionally, Almac leverages 2D bar scanning—tracked and monitored in its ERP/MRP system—to locate the product at all stages. The company has an interface accessible to its partners, empowering inventory traceability and distribution transparency and visibility across the supply chain.

Almac Adapt™: Production and Distribution Phase



Courtesy of Almac Clinical Technologies

The exceptional JTM solution aligns with the critical needs of its fast-moving environment while delivering substantial efficiency gains. Its adaptability to clinical trial requirements enables proactive actions without impacting patients, i.e., missing a dose, wasting materials, and adding timeline pressures to patient-specific clinical trials.

As a global solution, all of Almac's facilities, strategically-located for a quick response, offer this approach—Craigavon, the UK; Dundalk, the EU; Pennsylvania and North Carolina, the United States; and Singapore, covering Asia.

Strong Start, Promising Outlook

Given the customer-led development process, drug sponsors showed a high interest level, engaging with Almac in consultative work before even Almac Adapt™ technically launched. Within 6 months of reaching the market, the company had about 10 customers, a mix of biotech, big pharma and contract research organizations, adopting its JTM solution. At 9 months, the company's service engagements grew by over 50%, i.e., more than 15 clinical studies ranging from Phase I to Phase III trials. As of the end of FY21 we are supporting over 45 studies, ranging from PH1 to PH3 in various therapeutic areas including: Immunology, Rare Disease, Oncology, Respirology. Supporting companies in the Pharmaceutical & Biotech & Clinical Research Organizations sector.

As a member of an established CDMO, the Almac Adapt team caters to sponsor's various needs, offering multiple packaging and labeling strategies across one protocol. Pharma companies can leverage a hybrid approach, i.e., JTM and batch manufacturing, in response to

the specific challenges of particular clinical trial arms under the same protocol. Currently, Almac's partners mainly leverage Almac ADAPT™ in therapeutic classes such as cell and gene therapy, IO, and rare illnesses.

Frost & Sullivan notes substantial growth opportunity for innovation-driven CDMOs in the global clinical trial logistics and supply chain market segment, reaching approximately $2 billion in revenues by 2024.[8]

In particular, Frost & Sullivan is anticipating exponential Almac Adapt™ adoption due to the COVID-19 pandemic as drug sponsors, small and large, across the world race to develop the long-awaited SARS-CoV-2 vaccine.[9] With death tolls of over 211,000 people worldwide as of late April 2020,[10] time is of the essence, and sponsors can leverage JTM to accelerate vaccine development timelines.

Conclusion

The growth of biologics for precision medicine has led to manufacturing gaps. Development complexities and higher costs result in significant industry constraints as it relates to managing and meeting the current demand. Mainly, delays in biologics manufacturing through contract development and manufacturing organizations can take more than 18 months, tying up drug sponsors' multimillion-dollar investments in life-saving targeted therapeutic programs. Scheduling issues, process inefficiencies for small-volume high-value products combined with hyper-complex, patient-centered global supply chains are driving vendors to explore solutions for an uninterrupted clinical trial supply chain.

Frost & Sullivan recognizes Almac's just-in-time manufacturing (JTM) solution Almac Adapt™ as a truly disruptive innovation in the clinical trial supply chain. The company's pioneering JTM solution defers packaging and labeling until the need occurs. As such, the on-demand systematic process enables seamless, late-stage clinical trial supply customization, helping drug sponsors in optimizing global clinical trial supply management to 'Advance Human Health' cost-effectively**.**

With its strong overall performance, the Almac Group earns the 2020 Frost & Sullivan Global Company of the Year Award in JTM solutions for the clinical trials supply market.

[8] *Global Contract Research Organization (CRO) Market, Forecast to 2024 (Frost & Sullivan, November 2019)*
[9] *https://www.nature.com/articles/d41573-020-00073-5*
[10] *https://www.who.int/emergencies/diseases/novel-coronavirus-2019, Accessed April 30, 2020*

Significance of Company of the Year

To receive the Frost & Sullivan Global Company of the Year Award requires a market participant to demonstrate excellence in growth, innovation, and leadership. This excellence typically translates into superior performance in three key areas—demand generation, brand development, and competitive positioning—that serve as the foundation of a company's future success and prepare it to deliver on the 2 factors that define the Company of the Year Award: Visionary Innovation and Performance, and Customer Impact.

Understanding Company of the Year

Driving demand, brand strength, and competitive differentiation all play critical roles in delivering unique value to customers. This three-fold focus, however, must ideally be complemented by an equally rigorous focus on Visionary Innovation and Performance to enhance Customer Impact.

Key Benchmarking Criteria

For the Global Company of the Year Award, Frost & Sullivan analysts independently evaluated each factor according to the criteria identified below.

Visionary Innovation & Performance

Criterion 1: Addressing Unmet Needs
Criterion 2: Visionary Scenarios through Mega Trends
Criterion 3: Implementation Best Practices
Criterion 4: Blue Ocean Strategy
Criterion 5: Financial Performance

Customer Impact

Criterion 1: Price/Performance Value
Criterion 2: Customer Purchase Experience
Criterion 3: Customer Ownership Experience
Criterion 4: Customer Service Experience
Criterion 5: Brand Equity

Best Practices Recognition: 10 Steps to Researching, Identifying, and Recognizing Best Practices

Frost & Sullivan analysts follow a 10-step process to evaluate Award candidates and assess their fit with select best practice criteria. The reputation and integrity of the Awards are based on close adherence to this process.

STEP		OBJECTIVE	KEY ACTIVITIES	OUTPUT
1	**Monitor, target, and screen**	Identify Award recipient candidates from around the globe	• Conduct in-depth industry research • Identify emerging sectors • Scan multiple geographies	Pipeline of candidates who potentially meet all best-practice criteria
2	**Perform 360-degree research**	Perform comprehensive, 360-degree research on all candidates in the pipeline	• Interview thought leaders and industry practitioners • Assess candidates' fit with best-practice criteria • Rank all candidates	Matrix positioning of all candidates' performance relative to one another
3	**Invite thought leadership in best practices**	Perform in-depth examination of all candidates	• Confirm best-practice criteria • Examine eligibility of all candidates • Identify any information gaps	Detailed profiles of all ranked candidates
4	**Initiate research director review**	Conduct an unbiased evaluation of all candidate profiles	• Brainstorm ranking options • Invite multiple perspectives on candidates' performance • Update candidate profiles	Final prioritization of all eligible candidates and companion best-practice positioning paper
5	**Assemble panel of industry experts**	Present findings to an expert panel of industry thought leaders	• Share findings • Strengthen cases for candidate eligibility • Prioritize candidates	Refined list of prioritized Award candidates
6	**Conduct global industry review**	Build consensus on Award candidates' eligibility	• Hold global team meeting to review all candidates • Pressure-test fit with criteria • Confirm inclusion of all eligible candidates	Final list of eligible Award candidates, representing success stories worldwide
7	**Perform quality check**	Develop official Award consideration materials	• Perform final performance benchmarking activities • Write nominations • Perform quality review	High-quality, accurate, and creative presentation of nominees' successes
8	**Reconnect with panel of industry experts**	Finalize the selection of the best-practice Award recipient	• Review analysis with panel • Build consensus • Select winner	Decision on which company performs best against all best-practice criteria
9	**Communicate recognition**	Inform Award recipient of Award recognition	• Announce Award to the CEO • Inspire the organization for continued success • Celebrate the recipient's performance	Announcement of Award and plan for how recipient can use the Award to enhance the brand
10	**Take strategic action**	Upon licensing, company able to share Award news with stakeholders and customers	• Coordinate media outreach • Design a marketing plan • Assess Award's role in future strategic planning	Widespread awareness of recipient's Award status among investors, media personnel, and employees

The Intersection between 360-Degree Research and Best Practices Awards

Research Methodology

Frost & Sullivan's 360-degree research methodology represents the analytical rigor of our research process. It offers a 360-degree view of industry challenges, trends, and issues by integrating all 7 of Frost & Sullivan's research methodologies. Too often companies make important growth decisions based on a narrow understanding of their environment, leading to errors of both omission and commission. Successful growth strategies are founded on a thorough understanding of market, technical, economic, financial, customer, best practices, and demographic analyses. The integration of these research disciplines into the 360-degree research methodology provides an evaluation platform for benchmarking industry participants and for identifying those performing at best-in-class levels.

360-DEGREE RESEARCH: SEEING ORDER IN THE CHAOS

About Frost & Sullivan

Frost & Sullivan, the Growth Partnership Company, enables clients to accelerate growth and achieve best-in-class positions in growth, innovation, and leadership. The company's Growth Partnership Service provides the CEO and the CEO's Growth Team with disciplined research and best practice models to drive the generation, evaluation, and implementation of powerful growth strategies. Frost & Sullivan leverages more than 50 years of experience in partnering with Global 1000 companies, emerging businesses, and the investment community from 45 offices on six continents. To join our Growth Partnership, please visit http://www.frost.com.