ALMAC

Partnering to Advance Human Health

Customer Guide

# Almac's Cryogenic service solution

Next generation solutions for your next generation therapeutics

# By your side - supporting the drug discovery of tomorrow, today...

The Almac Group is a global leader in providing a range of expert services and support across the drug development lifecycle to pharmaceutical and biotech companies. We are trusted experts in R&D, diagnostic services, API manufacture, formulation development, clinical trial supply services and technologies through to commercial-scale manufacture and distribution.

We are recognised as an industry leader in client service, providing understanding, experience and knowledge to our clients as we work together to advance human health.
Almac is trusted by the leading global biopharma companies to provide crucial services across their drug development projects. In the last 5 years alone, we have contributed to approximately 50% of all FDA approved New Molecular Entities (NMEs) and are currently supporting 30% of EU approved /pre-registered Gene therapy products.

A privately owned organization, Almac has grown organically over the past five decades, employing over 6,500 highly skilled employees across 18 facilities in Europe, North America, and Asia.

## Right drug, right patient, right time, right temperature

Almac Clinical Services provides the most comprehensive global clinical supply chain solutions in the marketplace. Guided by our extensive clinical supply experience, we provide the physical resources and supportive technologies that ensure your clinical supply chain continually delivers across the globe.

At Almac we continue to invest in our capabilities, capacity and technology to deliver an innovative clinical supply solution for Advanced Therapy Investigational Medicinal Products (ATMP). The range of exciting, advanced therapies in clinical development continues to increase across the globe, demanding unique expertise and an end-to-end view of the complete clinical supply chain.

Clinical trial supply chains are becoming longer and more complex, while costs are rising and sponsors face additional challenges to reduce waste, cost and timelines. As trials become truly global, sponsors require partners that can provide the physical means of packaging, labelling, and distributing their supplies, as well as providing the data to facilitate planning and enable decision-making.

Harnessing our expert people, robust processes, and cutting-edge technology, Almac Clinical Services offers sponsors a fully comprehensive clinical supply chain solution that overcomes the increasing complexities of delivering the right drug, to the right patient, at the right time and temperature: safely, compliantly, and cost-effectively.

## Your next generation therapeutics – safe in our hands

At Almac, we are committed to exceeding customer expectations and supporting sponsors to maximise the potential of advanced therapeutics to drive forward new advancements in human health. As a world leading contract development and manufacturing organisation, with a global reputation for excellence built on 50 years of dedicated client service and expertise spanning the drug development lifecycle, Almac's Cryogenic Service Solution guarantees your next generation therapeutics are in the safest of hands.

The Cryogenic Service Solution extends Almac's specialist temperature-controlled offering; providing sponsors with a complete solution for the secondary packaging, storage and dispatch of cell and gene therapies, as well as other treatments that require highly specialised temperature control at cryogenic ranges.

*Removing risk from your complex supply chain*

Creating optimised and effective clinical supply chain services for advanced therapies is an incredibly complex, yet vital mission. The new addition to Almac's extensive service offering will serve to lower risk by offering sponsors an unbroken chain of custody.

Our cryogenic capabilities will combine with our market leading temperature-controlled clinical supply and logistics solutions, including packaging, labelling, distribution, storage and our logistics management platform, to provide a truly integrated clinical supply chain offering.

As a result, sponsors will obtain holistic visibility over clinical supply from production line to patient; enabling them to monitor shipments, track conditions, location, and handling of advanced therapeutics in transit around the clock and deploy intervention capability to mitigate potential risk.

*A tailored service you can trust*

In addition to a new flagship, state of the art cGMP Cryogenic processing suite at Almac's Durham, North Carolina, facility, at the centre of Almac's Cryogenic Service Solution is our unique service level.

This brings together dedicated project management resources, expert people highly skilled in on-demand production techniques, validated processes, and advanced technology.

Every Almac Cryogenic Service Solution is designed around the specific needs of sponsors, positions patients at the core of all decision making, and is delivered to maximise performance to uphold patient safety and compliance, ensure key study milestones are met, costs controlled and return on investment is maximised.

*What territories is the Cryogenic Service Solution available in?*

Currently available in the US, as demand continues to grow, as will Almac's investment in the future of human health. Using our Durham site as a blueprint, Almac will further increase operational capacity by replicating cryogenic capabilities at our other clinical supply services facilities within Almac's global network.

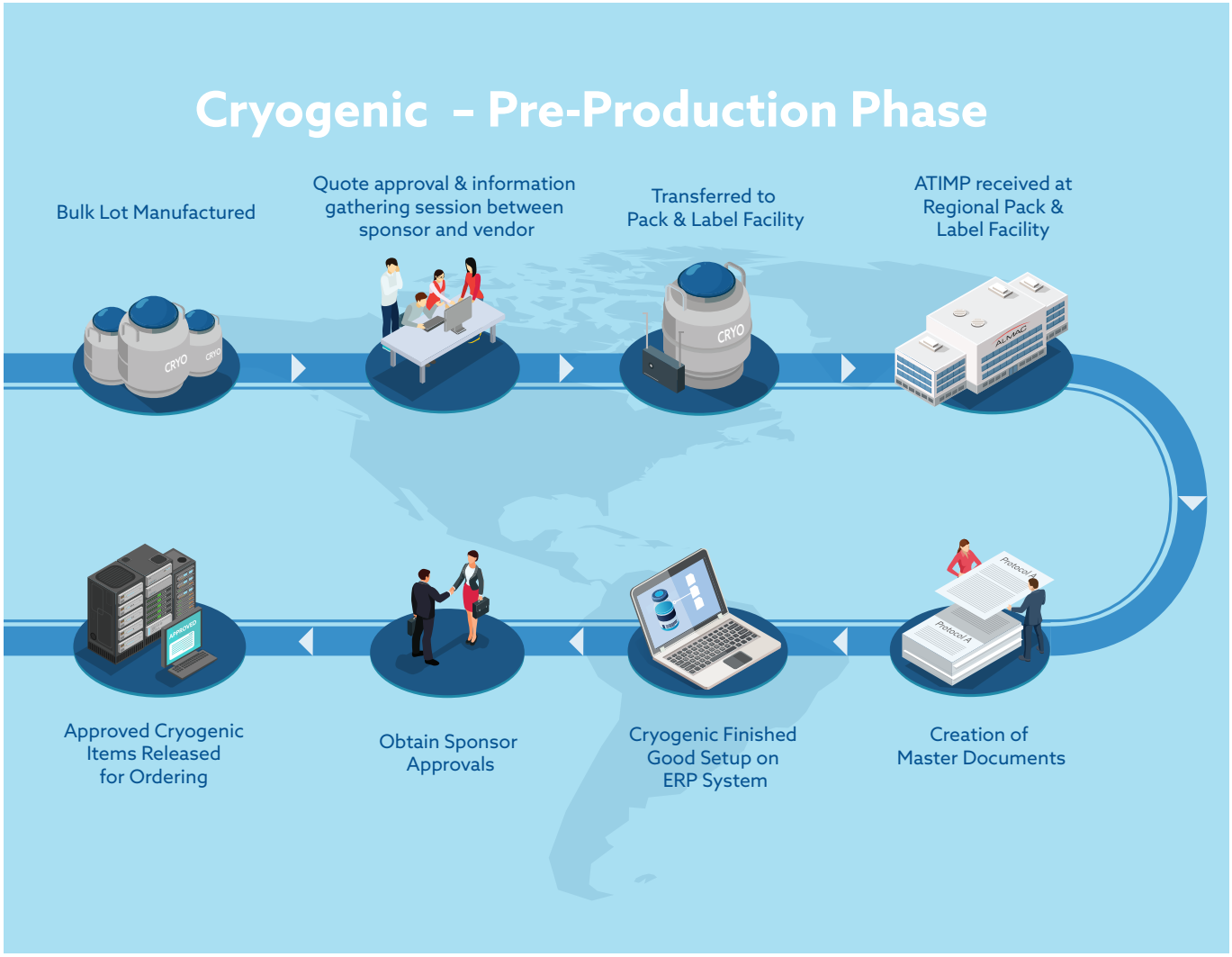
## Combine cryogenic capability with on-demand production

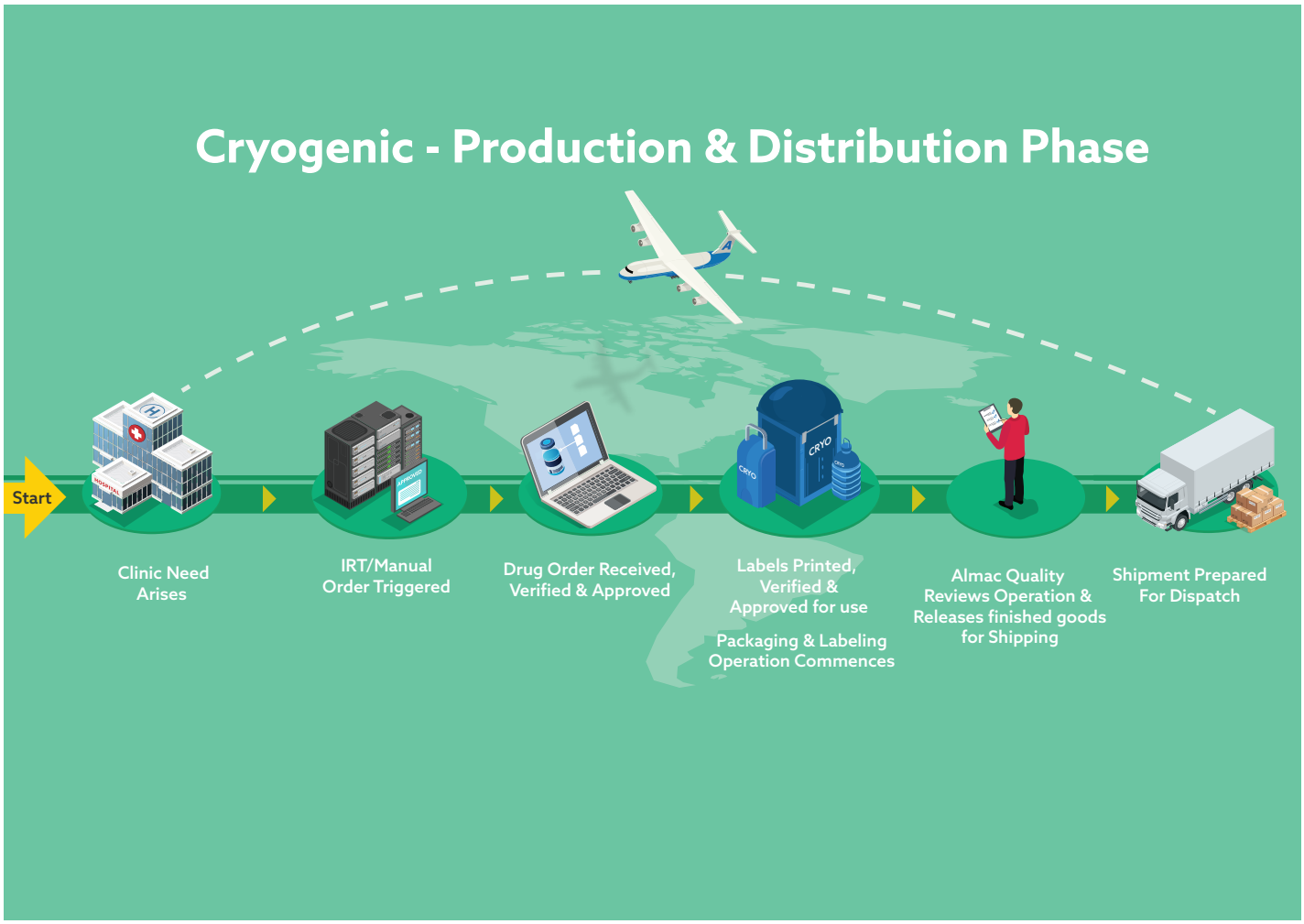
Maintaining appropriate handling of your precious cryogenic materials and minimising time out of condition is a top priority. Almac's Cryogenic Service Solution has been designed by experts in the handling of complex biologic materials and is built around a set of robust processes. These processes combine to prioritise product integrity, patient safety and cost-control from initial receipt of materials at the cryogenic facility through to shipment, dispatch and beyond.

Almac's Cryogenic Service Solution delivers an optimised and agile clinical supply chain that meets the continuously evolving needs of your clinical development team and patients alike.

Proven to deliver exceptional value in ambient, refrigerated, frozen and ultra-low conditions, the on-demand model has been tailored to accommodate cryogenic handling. As such, Almac's Cryogenic Service Solution enables the full late-stage customisation of clinical supplies by postponing packaging and labelling until the site or patient need arises.

Especially important for studies involving high cost, low yield next generation therapeutics, this production approach aligns speed with need through the clinical supply chain to empower sponsors to meet variable demand, while maximising supply and effectively controlling costs.






## Ensure a smooth pre- production phase for your cryogenic materials

Tailored to the unique requirements of sponsors and managed by a dedicated clinical supply chain specialist through each touch point, the pre-production phase of Almac's Cryogenic Service Solution incorporates a set of defined and validated processes that deliver seamless operations.

The process begins with the receipt of advanced therapeutic investigational medicinal product (ATIMP) at Almac's cutting-edge cryogenic secondary packaging suite. Once received, an information gathering session between Almac experts and key sponsor contacts takes place to discuss and understand study specifics before formalising subsequent steps.

Next, Almac uses this information to create Master Documents, set-up cryogenic 'finished goods' on the ERP system, before obtaining sponsor approval and releasing items for ordering.

With these key processes in place, the pre-production phase can be complete and studies distribution ready within days.

## Next generation facilities for your next generation therapeutics

The Cryogenic Service Solution includes equipment to safely handle, perform secondary packaging activities, and store cryogenic materials within a fully contained, cGMP compliant / audited suite with three segregated processing rooms.

Cryogenic freezers, with segmented racks to accommodate dedicated customer storage, are in place to hold 42,000 plus vials, with 100% redundancy factored in.

The ergonomically designed freezer is accessible from ground level, removing the need for operatives to climb steps and therefore reducing the likelihood of breakages, costly product rework, and negative patient impact.

These advanced facilities enable ATMP to be preserved in liquid nitrogen vapour between -150c and -196c temperature ranges, prior to distribution. The cryogenic shipping service will then utilise specialist vapour shippers and cryogenic boxes for dispatching product to customer destinations.

*Can I store my ATMP at Almac's Cryogenic facility?*

While storage is not offered as a stand-alone service, custom storage solutions to support client specific requests can be discussed.

*How will Almac guarantee security?*

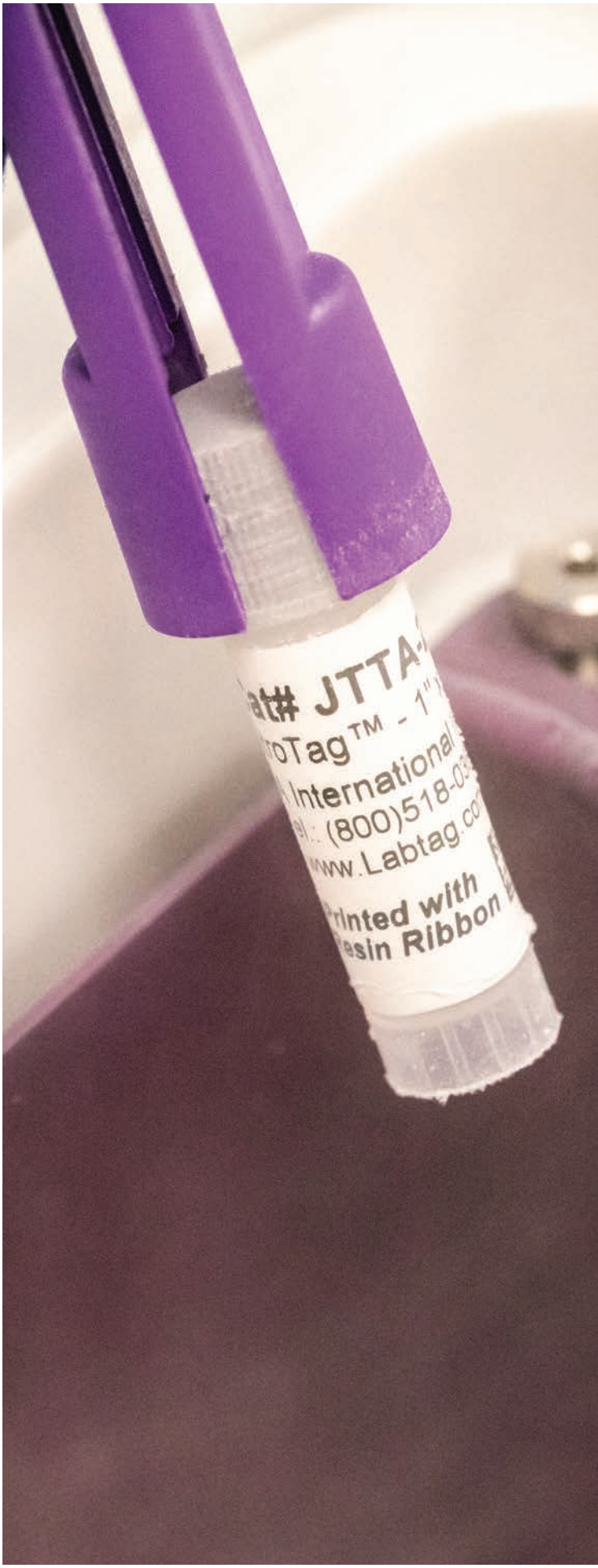
ATMP will be stored in a controlled space, within a highly secure cGMP, FDA audited facility with a secured entry badge to control access. The facility encompasses multiple layers of protection, including vapour phase, 24/7 surveillance and building management systems to continuously monitor vessels and environmental conditions. Individual processing suites will be controlled by further secured entry.

## Production & Distribution: Guarentee success with one seamless process

With the pre-production phase complete, the production and distribution phase can commence.

Almac's Cryogenic Service Solution optimises supply, while ensuring rigorous adherence to products' specific temperature requirements.

The production and distribution process offered as standard as part of Almac's Cryogenic Service Solution is driven by clinical site/patient demand and designed to provide a seamless mechanism to effectively process materials from site order through to shipment.



The process begins when an order is raised either via IRT or upon receipt of a manual Drug Order Form. In turn, this triggers the order of a cryogenic conditioned shipper. Operatives then schedule the cryo production job and await the arrival of the shipper at site before entering the cryogenic conditioned shipper.

The label work order is then raised and specialist kit labels, utilising materials designed to withstand cryogenic conditions, are printed, verified, and approved following robust QC processes. Labels are applied to kits as part of a qualified process in dedicated temperature-controlled suites, in accordance with cGMP requirements, designed to ensure efficiency and minimise time out of condition. This is achieved by harnessing tactics, including seamless, instantaneous transfer from condition requirements to pack stations using cryo-pods to mitigate risk and uphold product integrity.

Once verified CTM is ready to be placed into shippers, expert cryogenic production operatives perform the digital 'pick' in the Oracle system using mobile devices, before printing the drug issue and label issue forms and conducting QC verification of the mobile Oracle.

At this point, CTM is moved into the processing room using a cryo-pod. The batch record is then used to build the first unit, which goes through the QC process prior to conducting packaging activity in accordance with the batch record. Further QC checks are then performed before the finished kit is placed in a pre-charged cryogenic conditioned shipper.

When complete, a summary report is printed, and operations reviewed by dedicated quality personnel. With QC sign off in place, finished goods are released for shipping to the designated location and 'time out of conditions' validation conducted and processing rooms cleaned down ahead of the next packaging operation.

*How will Almac minimise time out of condition during the picking process?*

The Cryogenic Service Solution utilises two cryo-pods during the picking process. When cryo-boxes with the desired materials are selected, they are immediately placed into the first cryo-pod to maintain temperature conditions. The second cryo-pod, referred to as the incoming pod, is used to hold the material needed for the job, which is confirmed in advance by Quality Control personnel. Once the job is complete, the first cryo-pod is used to return the cryo-box to the vessel. Now empty, the first cryo-pod is used to store the preconditioned kit materials and facilitate safe handling of finished goods.

*How will Almac safeguard my ATMP in transit?*

To maintain precise temperatures through transit, Almac harnesses specialist dry vapor cryogenic shippers that utilise real-time GPS tracking and temperature monitoring, ensuring product is delivered on time and in specification.

Each shipment delivers full traceability via a report that can be accessed by the sponsor or the Almac Temperature Services team.

Other key features and benefits of the specialist cryogenic shippers include:

- High performance (temp: -196°C, static: 10+ days, continuous 90° tilt: 2.7-3.5 days)
- Innovative design delivers high performance in dynamic states, allowing shippers to be stored on their sides without failure and removing the need to palletise
- Generous payload capacity of up to 2x Cryobox (13x 13x 5cm) and multiple cassettes
- Controlled under a single global quality system
- Established cleaning and qualification SOPs

## Your partner of choice: yesterday, today, and tomorrow

Advanced therapeutics, and other biologics that require cryogenic handling, are transforming the face of modern medicine and creating new, ground-breaking possibilities for patients living with a vast range of conditions.

Effective management of clinical trial supply is central to maximising the potential of these wonder drugs, championing better health outcomes for patients, and contributing to the advancement of global human health. Without effective clinical trial supply strategy and precision cold chain capability, product integrity becomes 'at risk', key study milestones become harder to meet, and the associated costs are left spiralling out of control, compromising successful progression into subsequent trial phases and commercialisation.

While operating cryogenic clinical supply chains brings with it substantial complexity and risk, the concept of getting the right drug, to the right patient, at the right time and temperature remains unchanged.

With the correct foundations in place, supported by access to cryogenic supply chain specialists and advanced cryogenic facilities, the full potential of advanced therapeutics can be realised and return on investment secured.

## Find out more about Almac's Cryogenic Service Solutions

Email us at
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Or visit us on our website at
almacgroup.com.

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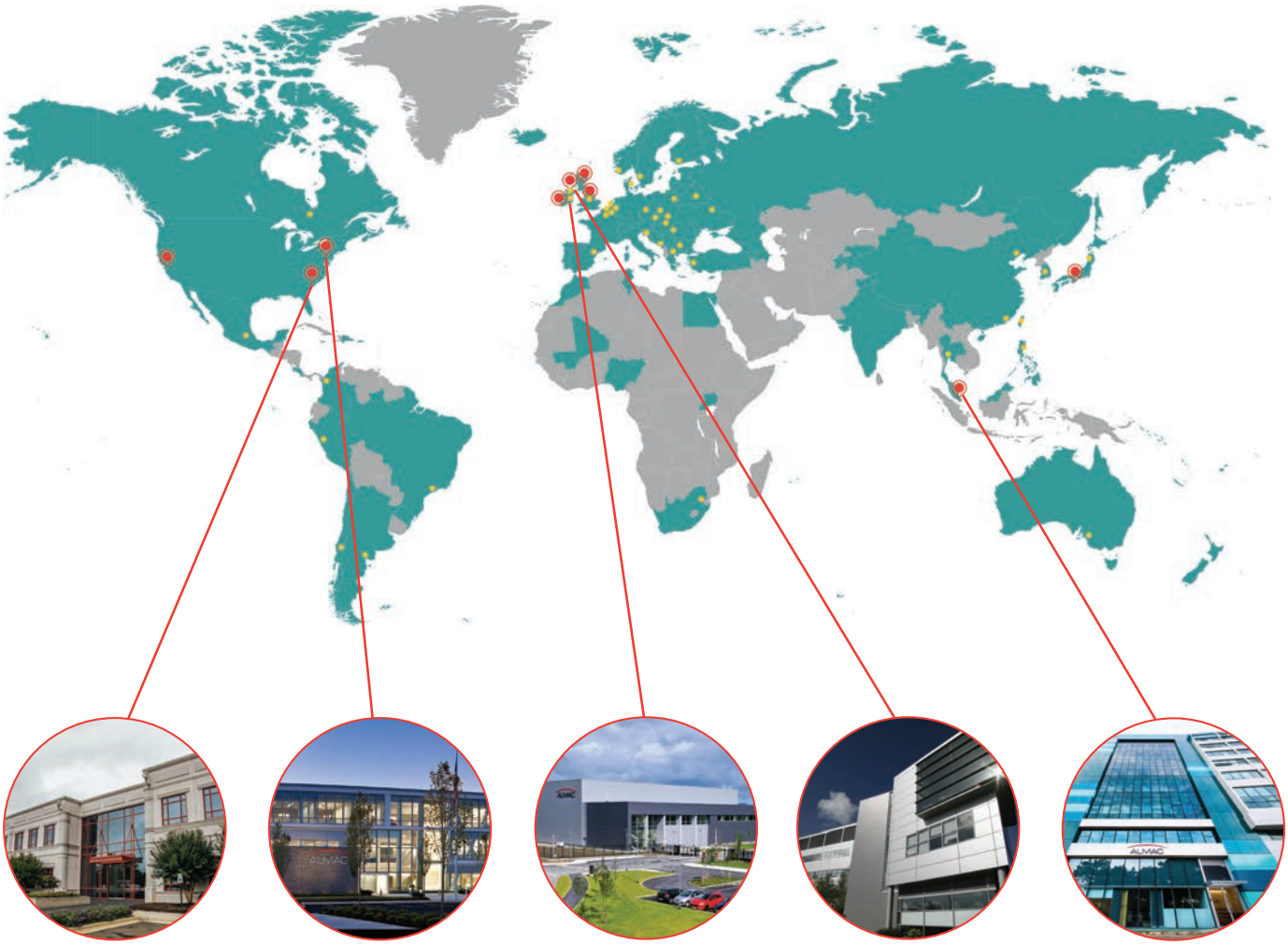
# Almac Global Presence





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Countries we have provided services to in the last 50 years

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