Building A Resilient Supply Chain For Your Next-Generation Peptide Therapeutic

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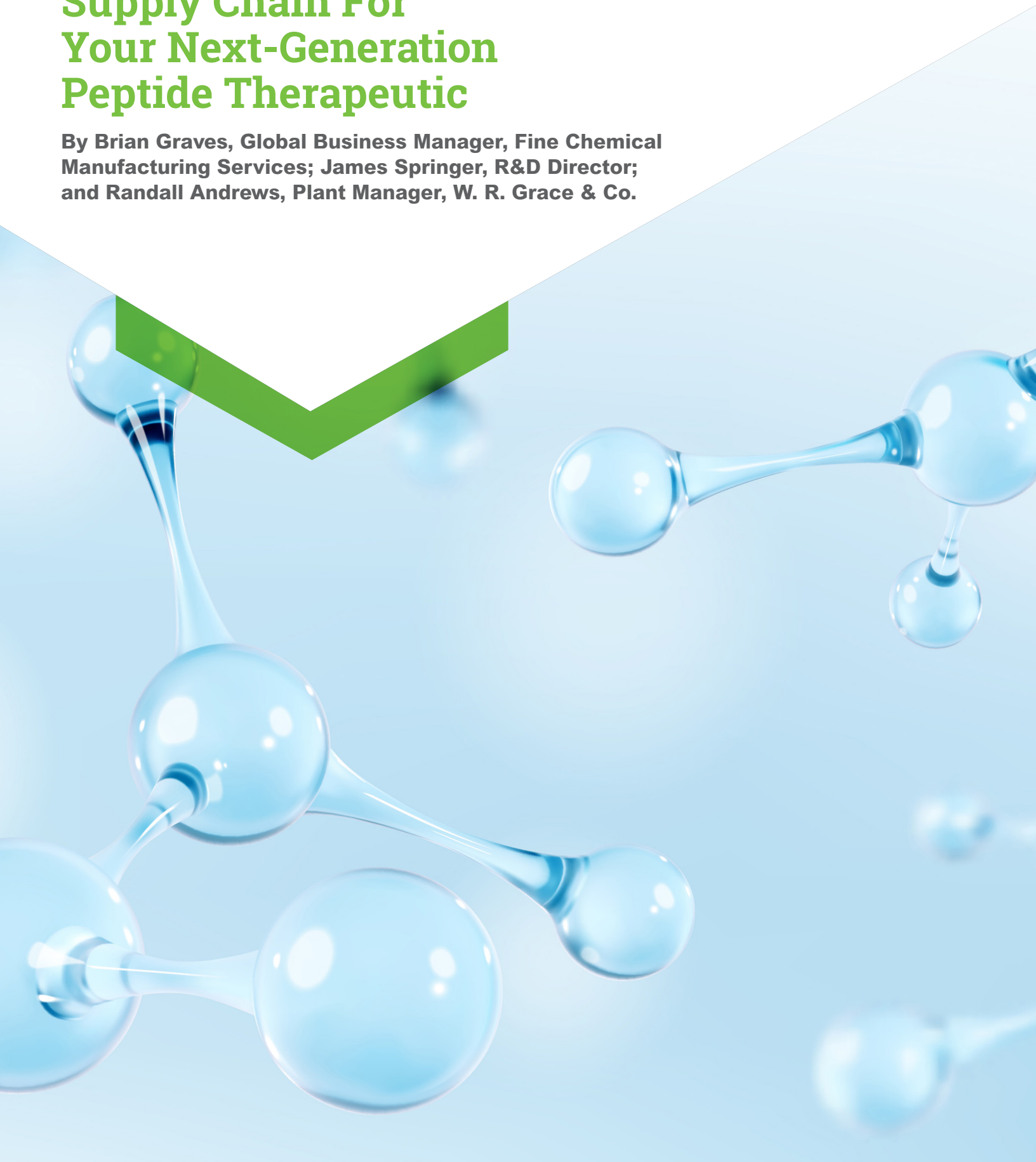

Amid the demand for more targeted therapies, peptide therapeutics have emerged as a leading technology and an innovative treatment option for indications such as cancer, obesity, and diabetes, to name just a few. These therapeutics offer an array of benefits, including high target specificity, low toxicity, and favorable safety profiles, all of which can be beneficial to patients who require long-term treatment for chronic disease.[1] One notable boon in the peptide therapeutic surge has been the continued success of glucagon-like peptide-1 receptor agonists (GLP-1 RAs), including semaglutide and tirzepatide. From 2022 to 2023, GLP-1 peptide therapy usage doubled for obesity treatment.[2] Currently used to treat type 2 diabetes and obesity, these therapeutics are being studied for a range of other potential applications.

According to a report by Mordor Intelligence, the peptide therapeutic market is expected to reach over $51 billion in revenue in 2025 and continue growing at a compound annual rate of 9.66% over the next five years.[3] To navigate this rising demand, drug sponsors must be diligent about mitigating drug shortages and ensuring a continuous supply to patients. A crucial component of this is establishing reliable partnerships, which includes a peptide building block supplier. Selecting the right supplier can help your team ensure a reliable supply of high-quality key starting materials.

Strategically Navigate an Uncertain Manufacturing Climate

As a result of the major offshoring push for pharmaceutical manufacturing in the ‘90s and early 2000s, the majority of peptide building block suppliers are in the Asia-Pacific (APAC) region where labor costs are lower. In the years when the peptide surge was gaining momentum, a variety of APAC companies, particularly in China, became reliable producers of the precursor materials needed for peptide manufacturing. However, in more recent years, concerns about the reliability of procuring raw materials from the APAC region have risen.

In part, these uncertainties are the result of ongoing geopolitical tensions. The U.S. government is working to pass the Biosecure Act through Congress, seeking to limit federal agencies from working with or funding a “biotechnology equipment or service” from a “biotechnology company of concern.”[4] A company of concern is defined as one that “engages in joint research with, is supported by, or affiliated with a foreign adversary’s military, internal security forces, or intelligence agencies; provides data obtained via biotechnology equipment or services to the government of a foreign adversary; or obtains human data via biotech equipment or services without express and informed consent.”[4]

It is important to consider the potential implications of sourcing critical raw materials from companies that may be affected by growing geopolitical challenges, including regional conflicts impacting trade routes, the potential for sanctions and embargos, and legislative actions like the Biosecure Act. There is also the growing likelihood of tariffs levied on imported goods, a proposed strategy by the incoming Trump administration to bring manufacturing back to the U.S.[5] These tariffs could have a negative impact on the budgets of any U.S. companies that opt to outsource manufacturing to non-domestic partners and further increase the uncertainties surrounding offshore supply.

Amid these ongoing geopolitical concerns, it is important to identify a partner that is not only geographically accessible but that offers the expertise to accommodate a wide array of complex building blocks. While there are only 20 canonical amino acids, there are an infinite variety of other peptide building blocks that might be needed to create a specific therapeutic. This includes difficult to produce and source non-canonical and non-natural amino acids and small peptides that may be useful in reducing the cost of a solid-phase synthetic approach or adopting liquid phase or hybrid manufacturing strategies. To manufacture these building blocks successfully, you will need a supplier that is well versed in the variety of chemistries and approaches to synthesizing these unique compounds.

Consider Manufacturing Challenges

One of the major challenges for manufacturing peptide building blocks is controlling impurities. Manufacturers must have the capabilities to identify, measure, and remove impurities, because these compounds often have strict impurity profile requirements. Some impurities may be introduced through raw materials while others may be the result of process conditions. By knowing the origin of these impurities, a supplier can develop a plan to mitigate their formation and purge them via crystallization or extractions. In most cases, peptide building blocks are chiral compounds and may contain multiple chiral centers. Properly characterizing all the possible chiral and diastereomeric impurities early in development is crucial to avoid problems down the road.

Though many are alike, each amino acid is unique, which can create unique challenges. For example, alanine, glycine, and isoleucine can be relatively similar; however, subtle structural variations can lead to surprising differences requiring distinct strategies for purification and isolation. More complex challenges arise from residues with orthogonal functionalities and differentiating protecting groups on side chains. Therefore, it is vital to enlist a partner knowledgeable in amino acid chemistry who understands your project's specific requirements and is well-equipped to navigate synthesis, purification, and quality requirements.

Internationally harmonized guidelines recognize that the manufacture of starting materials, such as simple functionalized amino acids, are not subject to specific pharmaceutical GMP conditions. However, more complex materials, such as small peptides or particularly unique peptide building blocks, may be classified inconsistently by regulatory agencies and thus may have divergent GMP manufacturing requirements. This should be considered early in development and factored into partner selection.

Rely on a Proven and Experienced Partner

A well-honed approach to manufacturing custom peptide building blocks involves a detailed review and analysis of the customer's specifications, including their intended application and impurity requirements. The process should engage a team of knowledgeable chemists who have a deep understanding of the chemistry required to produce the raw materials and the eventual application of the peptide therapeutic, as well as leverage an integrated cross functional approach to provide holistic program support to maintain a seamless workflow, mitigate risk, and ensure timeliness.

For example, at Grace Fine Chemical Manufacturing Services (FCMS), in the initial phases of a project, our team works to develop a broad knowledge base of the customers' requirements and intended scope of work to develop a project proposal. Following this stage, our R&D team steps in to create a scalable process that can run in our plants while collaborating with chemical engineers along the way to ensure that our chemistry and equipment capabilities are well aligned and scalable. Our teams also conduct safety studies to ensure that the processes are safe to operate. Finally, our analytical services experts develop quality methods to analyze each stage of a process to guarantee quality and robustness.

Aligning with a partner who offers flexibility and can accommodate your specific program structure is essential – this should be a collaborative exercise and your level of involvement will depend on the nature of your unique program and comfort level. At Grace FCMS, we welcome clients to visit our sites, conduct audits and engage with our teams, especially in function-to-function collaboration, to enhance the overall process.

Control The Controllables

Ensuring impurity control requires via robust processing understanding and can be achieved by leveraging a Quality by Design (QbD) approach, which integrates technology, fully characterizes every step of the process, and anticipates obstacles. Grace offers two FCMS manufacturing sites in the United States: one in Tyrone, Pennsylvania, and another in South Haven, Michigan, both of which offer full functional quality laboratories with similar instrumentation that can easily be transferred between the two. Our South Haven site is an FDA registered cGMP site, and our Tyrone site is a non-GMP site that aligns with basic cGMP guidelines and produces regulatory starting materials (RSMs) for API products. We offer ample capacity to meet customer demand and can produce multiple tons of different compounds in GMP or ISO conditions, depending on the requirements.

An advanced analytical toolkit is fundamental for identifying specific concerns for amino acid derivatives and peptide building blocks. Technologies such as liquid chromatography-mass spectrometry (LCMS), nuclear magnetic resonance spectroscopy (NMR), X-ray crystallography (XRD), and methodologies for understanding crystallizations, such as solid-state probes and automated reactor systems, are also critical. Due to the scrutiny around the existence of multiple crystal forms, it is important to assess how these crystals behave differently via analytical technology. Ultimately, this understanding is critical to successful manufacturing and scale-up.

Securing critical raw materials from reliable partners and maintaining a network of multiple vendors is crucial and should ideally include vendors from different geographies. Ensuring partners and vendors meet EHS, manufacturing, and quality standards, and that they adhere to requirements around fair and responsible sourcing practices is vitally important.

Choose High-Quality Partners For Your Peptide Therapeutic

As peptide therapeutics continue to establish themselves as a leading technology for treating chronic indications, it is vital for drug sponsors to identify reliable peptide building block suppliers to secure high-quality starting materials for their products. As you begin your search for a partner, it is important to weigh the risks associated with procuring your supply from the APAC region, but beyond that, consider partners that have the experience, expertise, manufacturing capacity, and analytical capabilities to support your journey to delivering therapies to patients as safely and reliably as possible.

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About the Authors

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About Grace Fine Chemical Manufacturing Services

Grace's Fine Chemicals Manufacturing Services (FCMS) is a leading North American CDMO and a full-service provider of fine chemicals to the world's leading companies across the pharmaceutical, agrochemical, and specialty materials markets. Grace FCMS helps global customers complete successful projects through a powerful combination of proven chemistry expertise, game-changing process development, high-quality custom manufacturing and exceptional service. Our strategically located facilities in South Haven, MI, and Tyrone, PA, enable us to be a fully integrated domestic partner for the development and manufacture of regulatory starting materials (RSMs), intermediates, and custom active pharmaceutical ingredients (APIs). From innovative R&D to commercial-scale production, we deliver the knowledge, experience, resources and service needed to move products to market faster and accelerate business.

For more information, visit **grace.com/finechemicals**

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