Quotient Sciences

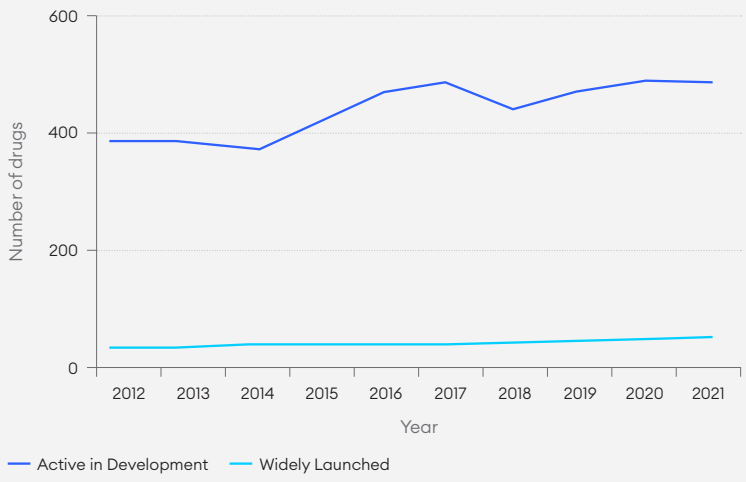
Molecule to cure. Fast.™

Information sheet

Peptide Development Strategies

Peptide drug products continue to gain popularity in the pharmaceutical industry due to their high selectivity, high potency, and good safety profile. However, formulating peptides can present many challenges for drug developers because of their unique physicochemical properties. As polymers of amino acids, peptides occupy a therapeutic niche between small molecules and large biologics. They are typically water soluble, hydrophilic, and charged, so they are poorly absorbed across the skin and mucosal membranes, making systemic delivery via routes other than injection challenging. In addition, the environment within the gastrointestinal (GI) tract is naturally geared to the digestion of peptides and proteins, presenting additional challenges for oral delivery.

Synthetic Peptide Drug Trends by Development Status



Our Expertise

- Peptide characterization and pre-formulation
- Biopharmaceutics profiling to guide route of delivery and formulation strategy
- Preclinical and clinical formulation development & formulation optimization
  - Oral, parenteral, inhaled, nasal, topical, rectal, and vaginal delivery
  - Regional delivery of oral peptides
- Phase I clinical assessment
  - First-in-human (FIH) studies
  - Relative bioavailability studies to optimize drug delivery technology performance
  - Absolute bioavailability studies
  - Bioanalysis

We base our approach to formulation development and analytics on the physical, chemical, and biopharmaceutic properties of each peptide and build a robust early development program that will meet Investigational New Drug Application (IND) and other regulatory requirements.

At Quotient Sciences, we understand the fundamental physiological challenges to peptide delivery and that there is no “one-size-fits-all” approach in regard to formulation design. With over 30 years of experience, our scientists have worked on a wide variety of peptide programs for a range of delivery routes involving both non-proprietary and proprietary third-party formulation technologies. We have significant experience in developing strategies to reduce both degradation and instability while maximizing absorption and bioavailability. With development and manufacturing services spanning the entire development pathway, we can support your program from candidate selection to commercial launch.

Services Spanning the Development Pathway

Lead Candidate Selection

In the candidate selection phase, we develop an experimental plan that is tailored to suit the stage of development and the availability and purity of the drug substance, often using material-sparing approaches. The outcome of this work is a recommendation on a lead molecule and a drug delivery strategy to pursue for in-vivo animal studies. Quotient Sciences can support:

- Analytical development using appropriate techniques
  - LC-MS
  - Reversed-phase HPLC/UPLC with UV, size-exclusion, and CAD detection
  - Light scattering methods
- Chemical stabilization (solid and solution state)
- Assessment of aggregation & binding
- Characterization in biorelevant conditions
- In-vitro permeability assessment

Preclinical Development of Peptides

Peptides often present unique stability and permeability challenges and so require a well-designed and adaptive plan for preclinical in-vivo screening and safety assessments. Our expertise includes:

- Solution development for oral and intravenous (IV) dosing
- Animal model selection appropriate for the drug delivery strategy
- Permeability enhancement by use of excipients and targeted drug delivery
- Safety assessment and dose selection of permeation enhancers

Clinical Development of Peptides

Clinical performance of a peptide can deviate from the outcome predicted by preclinical data. For non-parenteral routes such as oral and nasal, a complex formulation approach may be required for the FIH trial. Our scientists have experience with:

- Formulation design for a wide range of FIH dosage forms
- Adaptive clinical trial design solutions that allow dose strength and/or functional excipient selection based on emerging pharmacokinetic (PK) data
- Use of controlled-release coatings and permeation-enhancing excipients for oral, nasal, and other non-parenteral formulations
- Imaging using gamma scintigraphy to evaluate dosage form performance in the GI tract
- Sterile manufacturing of peptide products for IV, intramuscular (IM), or subcutaneous (SC) injection

Integrated Strategies for Accelerated Peptide Development

At Quotient Sciences, we offer standalone or fully integrated drug product development and clinical testing services for peptide programs. Our unique integrated platform, Translational Pharmaceutics®, accelerates drug development by integrating formulation development, real-time adaptive manufacturing, and clinical testing, all at one organization. When integrated, these services offer a single supply chain, led by a single project manager, under a flexible clinical protocol with rapid "make-test" cycles, where drug products are manufactured, released, and dosed in days or weeks rather than months, thus shortening the time to clinical data. Informed decisions are driven by human data, which not only optimizes the formulation but also multiplies the likelihood for formulation success.

The benefits of Translational Pharmaceutics' flexibility are particularly important for the delivery of peptides via alternative routes given the acknowledged lack of predictive non-clinical, in-vitro, or in-silico models. The ability to deliver peptide drugs via alternative routes can be efficiently assessed and formulation levels of drug and functional excipients can be optimized both to maximize bioavailability and minimize the cost of goods.

Key applications include:

- Accelerating molecules from FIH to proof of concept (POC)
- Selecting and optimizing clinical formulations
- Optimizing formulations to minimize injection site reactions
- Managing route switches from parenteral to alternative routes such as oral delivery

Translational Pharmaceutics has now been used by both large pharmaceutical and biotech companies on over 500 drug programs. A recent study by the Tufts Center for the Study of Drug Development revealed that Translational Pharmaceutics saves over 12 months of development time and at least $200 million in R&D costs compared to the traditional drug development paradigm.

Injectable route switch for peptide formulation optimization

Stealth BioTherapeutics, an innovative biopharmaceutical company based in Massachusetts, USA, was looking for a drug development partner to reformulate their peptide drug. Their molecule had demonstrated POC in early clinical trials with an IV formulation. However, with multiple indications under consideration, and with some requiring patient self-administration, there was a real need to transition from an IV to a SC formulation. Utilizing Quotient Sciences' Translational Pharmaceutics platform, a formulation design space was used to evaluate the safety and tolerability of SC administration and to see if target exposure via a new route could be achieved while minimizing injection site reactions. The design space allowed for flexibility to increase dose by concentration or volume. Drug products were manufactured in real time during the clinical study, and formulation compositions were informed by arising PK and tolerability data. A clinical study was performed on healthy volunteers testing six different formulation and dose variables, in which an SC formulation was selected that matched the IV AUC. Quotient Sciences was able to complete this program of work for Stealth within less than 7 months of CMC (chemistry, manufacturing, and controls) initiation.

Investigating oral peptide delivery using gamma scintigraphy

NovoNordisk was developing an oral formulation of semaglutide and wanted to understand the relationship between tablet disintegration and PK in human subjects. Quotient Sciences performed a gamma scintigraphy study by labeling the oral tablets with indium-111 and labeling the water with technetium-99m to outline the stomach. We then performed a two-way randomized cross-over study in 24 healthy volunteers that assessed the anatomical location of the tablet at the time of disintegration and GI transit using gamma scintigraphy. The study found that the tablet containing the oral peptide eroded in the stomach irrespective of water volume and that dosing in the fed state further reduced exposure. The lower fluid volume resulted in a reduced rate of tablet erosion, slower gastric emptying, and 70% higher AUC and C_{max} levels. Our scientists concluded that, in order to have clinically relevant exposure, the tablet must be administered in the fasted state. The study also provided data indicating that the peptide was being absorbed from the stomach, which was a significant discovery.

Who is Quotient Sciences?

Quotient Sciences is a drug development and manufacturing accelerator providing integrated programs and tailored services across the entire development pathway. Cutting through silos across a range of drug development capabilities, we save precious time and money in getting drugs to patients. Everything we do for our customers is driven by an unswerving belief that ideas need to become solutions, molecules need to become cures, fast. Because humanity needs solutions, fast.

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