"An Integrated Approach to Early Phase Clinical Development"

A new, integrated approach – RAPIDD™- is being applied to early phase clinical development, including complex peptide drug candidates

The average time to develop and launch a new drug product is typically 12 – 16 years. With only 1 out of each 5,000 drug candidates reaching the market and typical drug development costs in excess of $1 billion, this product development has historically been undertaken by large pharmaceutical companies. These companies had the capability, facilities and finance to support the drug development cycle from discovery to launch entirely in-house. Project timelines, and associated financing, were large in scale and long in duration. Most of the products in development pipelines were small molecule NCEs. A significant investment was often made in carrying out CMC development up front, prior to initial clinical trial phases. However, the landscape of the pharmaceutical industry is now changing and the classic model of pharmaceutical development is shifting.

These days it is not uncommon for drug candidates to be developed by small biotechnology and virtual companies. These smaller companies guide their small portfolio of products through the early development cycle, often with the specific aim of out-licensing the product after early phase clinical success. For a biotech, time horizons are focussed around financing milestones. The near term objective is generally to bring a new molecule from initial discovery through to phase I as rapidly as possible. With further investment to proceed to subsequent clinical phases or out-licensing following at a later stage, projects are financed by investors and development is often driven by the availability of finance. Ongoing financing is milestone driven with Phase I success as a key milestone. In this context, a focus on development time is key, with a strong need to maximise the value derived from existing finance.

Service Providers

The shift from big pharma in-house development towards smaller biotechnology and virtual companies means that many services traditionally carried out in house are nowadays outsourced.

For a typical new drug development programme, many diverse development activities must be covered. Typically, entry to Phase I encompasses API synthesis, physical form selection, drug product formulation development and production, stability trials, ADME, pre-clinical safety pharmacology, and regulatory submission.

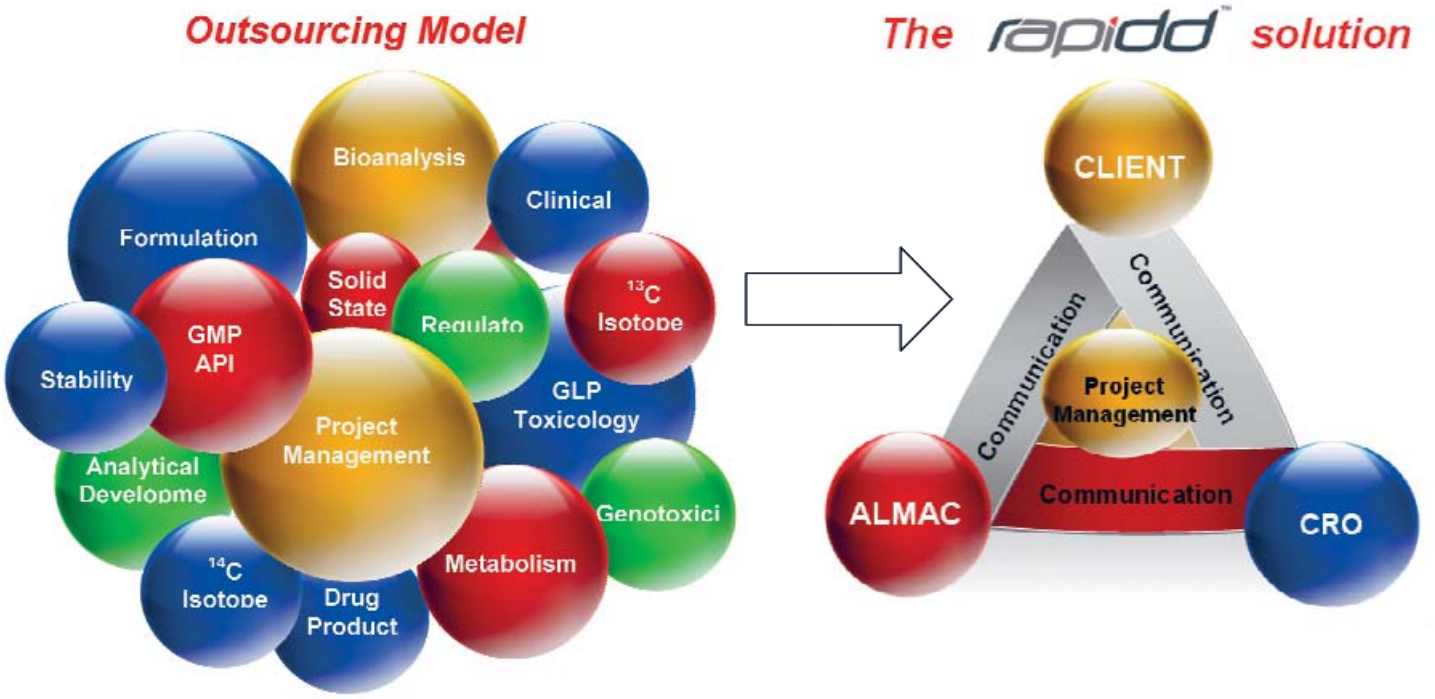
Each development activity is a specialist area, with its own particular requirements for expertise and infrastructure. Services are offered by many companies, each providing a stand alone service from different facilities in various global locations. Each product type - for example peptide APIs, multi-component vaccine cocktails, or small molecule NCEs - also has its own niche requirements. The procurement, scoping and management of such an array of outsourced services is a significant undertaking which draws heavily on the resources of the product owner. The benefit of having a single point of contact from a service provider who has the expertise to deliver an integrated development package can not be underestimated.

Almac Expertise

Almac has been a global service provider to the pharmaceutical industry for over 20 years. From its head quarters in the UK, Almac offers API process development and cGMP manufacture, pre-formulation development, Drug Product development and cGMP manufacture, clinical trials packaging, labelling and distribution. Almac has expertise in small molecule manufacture, radio-labelling, bio-catalysis, peptide synthesis and solid state chemistry. Almac also offers cGMP synthetic peptide development and manufacture, building on its existing deep expertise of peptide synthesis. Solid phase peptide synthesis technology is used by Almac to produce high purity peptides. At present, for research use, peptides of 200 amino acids in length have been made by solid phase synthesis. For pre-clinical and early phase clinical research application, a diverse array of peptide products have been manufactured in our production facilities including peptide-small molecule conjugates, radio-labelled peptides, synthetic peptide APIs, and multi-component peptide 'cocktail' products. Almac's customers benefit from having these services on one campus under the management of a Senior Project Manager dedicated to the integrated drug development program.

RAPIDD ™ (Accelerated Process Integrated Drug Development)

Almac offers a fully integrated service package – RAPIDD™ - enabling rapid entry to Phase I clinical trials. It has extended its own in house service capacity by forging partnerships with leading Contract Research Organisations. These carefully selected CRO partners are able to provide post CMC services including toxicology, safety pharmacology, ADME and regulatory support. The entire package from early route development through to regulatory submission is managed by Almac, with continual, open communication in place between all parties. This RAPIDD ™ integrated model enables the drug developer to benefit from a single point of contact, simpler communications, and a much reduced outsourcing management effort.



Development Strategy

Almac has significant expertise in drug product development, gained from years of experience of working with over 600 pharmaceutical companies ranging in profile from virtual to large pharmaceutical. Each year, on average, approximately 20 Phase I projects are handled through the Almac infrastructure. During this time, a significant collective of product development experience has been gained from handling a wide variety of products that includes small molecule NCEs, complex peptides and radio-labelled products. This experience enables Almac to have a balanced overview of the extent of development required for a new product, and to select appropriate partners for specific project requirements.

RAPIDD™ affords, as the name suggests, rapid drug development. At project commencement, the client company and Almac scope the project requirements from early route development through to expected clinical trial shape. A careful, fully integrated plan is agreed, which removes duplication of work, unnecessary contingency planning and technical transfers. Analytical methods, for example, are harmonised from the outset to enable their application to API, Drug Product and all supporting stability studies. Communication between technical teams is paramount, with all partners being aligned to the same goal – namely a rapid, lean development programme and fast entry to Phase I. Significant time savings can be gained for example by implementing a focussed development programme and manufacturing in a single campaign material for pre-clinical activities and cGMP use. The client's preferred development strategy is discussed and agreed at the project commencement with the client.

Proven approach to drug development

There has been a positive response to the concept of integrated services. A number of integrated projects have been successfully delivered and others are in progress. In the small molecule area, a radio-labelled Investigational Medicinal Product has been produced for clinical trial use, by bringing together the diverse expertises of route development, manufacturing and cGMP production of radio-labelled Drug Product. In peptide services, completed integrated projects include the route development, cGMP production and Drug Product manufacture of a folded chemokine for Phase I use. More complex projects are currently in progress and encompass the full RAPIDD™ package which includes API manufacture, pre-formulation studies, formulation development, drug manufacture, and pre-clinical safety pharmacology programme management. The RAPIDD ™ model is being applied to a number of projects including a synthetic peptide vaccine of over 100 amino acids in length.

Adding value, speeding up delivery

A fast and smart approach is required to help reduce development costs; Almac is uniquely positioned to offer this service by integrating the development process across functions and on one site. The RAPIDD™ integrated package offering added value and rapid Phase I entry to our clients, is now effectively being applied to peptide, as well as small molecule programmes, to the benefit of Almac clients.

Author Profile

Dr. Hazel Moncrieff is Senior Group Leader at Almac, responsible for cGMP peptide manufacturing.