



Rapidd Fire

Almac Sciences will use CPhI Worldwide 2009 to launch a unique new service. We met with Denis Geffroy, VP of business development, to find out more.

For the Almac Group, this autumn has been a time of big news. First, chairman and founder Sir Allen McClay announced that he is handing over part of the company to plough profits into a charitable trust that will support research into cancer and other diseases by academics and industry, then came the news that the company had secured permission for major expansion plans that could lead to the creation of over more 500 jobs during the next five years.

Almac announced in early October that it had acquired a 2.2-hectare site at its headquarters in Craigavon, Northern Ireland, and it will begin the first phase of development there shortly. This will house a three-storey office unit for over 220 staff, while the second phase will see a new research facility and a new distribution unit added.

All this follows on from about €11 million investment in a new laboratory block and a specialist cold storage facility for clinical trial materials and much more on a new headquarters in North America as the company continues to expand. Employee numbers rose by 15% to 1,426 in the UK and 762 in the US last year and 128 new graduate and research positions in early 2009.

For Almac Sciences, one of five main divisions within the group, though, the main news will be the hard launch of Rapidd. This will be the key feature of its stand at CPhI Worldwide in Madrid this month.

Rapidd is not totally new, strictly speaking. Brochures were circulating at events since April. However, says Denis Geffroy, VP of Business Development for Almac Sciences, that was the 'soft' launch; this is the 'hard' launch, announcing Rapidd as an early phase development service available to customers throughout the pharmaceuticals and biotechnology sectors.

Rather than go in with all guns blazing, Geffroy explains, the company made a preliminary announcement and, since March, has been trialling the concept. It has now used Rapidd to bring a pre-clinical project to Phase I trials for a medium-sized pharmaceuticals firm, achieving in this in 11 months rather than the usual 18-24, though it would not want to tout 11 as typical. Three more projects are ongoing.



With this success behind it, the company is ready to bring Rapidd to a more formal market launch. But what exactly is Rapidd anyway?

The name, Geffroy says is (almost) an acronym. It stands for **A**ccelerated **P**rocess **I**ntegrated **D**rug **D**evelopment; the 'R' is tacked onto the front to emphasise speed. It has now been trademarked, with the strapline 'A complete set of solutions aimed at accelerating entry into clinical development'.

Any pharmaceuticals or biotechnology firm wants a drug it has in development to get to launch as quickly as possible, because every day lost is a day of patent life that can never be recovered. However, the process is not just time-consuming but often inefficient, especially during the early phases. The aim of Rapidd is to cut out these inefficiencies.



"In general, Almac Sciences is involved in about 20 Phase I projects per year – about the same as a typical medium-sized pharma company, though of course we don't own the products," Geffroy says. "Through this, we have learned a lot about the process. We used to be rather reactive, with clients using us as an outsourcing house. Now we have taken a different stance."

For the small and medium-sized pharma companies and virtual biotechs, who have long come to Almac Sciences for advice or even formal consultancy services on how to get to Phase I as quickly as possible, there is perennial problem: how much work should they do to get a compound to Phase I?

Often, they do far more than they need to, wasting time and money in the process, because they fear – often correctly – that regulators or, more likely still, the Big Pharma companies they will ultimately sell the compound to will demand that more tests be done. Doing too little, is of course, potentially disastrous.

Such firms lack the deep pockets, product champions and wariness of public attention that characterise Big Pharma. For them, speed is of the essence because getting to Phase I will probably trigger milestone payments, or they may simply be in need of cash as capital gets harder and harder to access. Moreover, the compound in question may be the only one they have.

How can companies work out how much is neither too much nor too little, when the rules are so opaque? This is where Almac aims to come in. "Each client is different. Our approach is to be a partner and collaborator, to find out where they want to go and manage the project to get it into Phase I trials as quickly as we can," Geffroy says.



Geffroy - Almac moving from reactive to proactive approach

Fine but, one might ask, is all this not just putting a brand name on common sense and market knowledge? Geffroy argues that Rapidd is much more than that and explains how it actually works in practice.

As John Patterson, former R&D director at AstraZeneca famously observed, there are three main barriers to success in pharmaceutical R&D, which are combining to make the whole process "a mess":

- **Time:** it takes 12-16 years to develop a new medicine
- **Cost:** it costs \$1 billion to bring one drug from concept to market
- **Attrition:** only one in 5,000 NCEs makes it to market

Rapidd addresses each of these issues, though time is really the key one, because saving time in this business by definition saves costs. Attrition, to some degree, follows; Rapidd cannot make a blockbuster out of a weak candidate but it can, through the integrated application of services, weed out failures or resolve critical issues quickly.



"An increasing number of drugs heading into Phase I trials are insoluble. At Almac we have a good group in solid-state who can work to improve solubility and availability," Geffroy says. "A lot of drugs are abandoned because of poor solubility, now we have the technology to revive them."

Typically, he adds, Big Pharma has all or most of the capabilities needed to get a compound through pre-clinical trials, often within one project team on one site. These usually include project management, formulation, toxicology, metabolism, drug product, ¹³C and ¹⁴C isotope labelling, stability, formulation, bioanalysis, solid state analysis, GMP API manufacture, etc. This has the obvious advantages of continuity.

With the rise of the outsourced model and the virtual pharma company, these capabilities are dispersed over many companies and many locations. The advantages here are keeping fixed costs down and improved flexibility. However, it has its drawbacks too: geographical separation between partners, multiple communication lines, limited scientific capabilities and limited teamwork.

"It can be very complex work for a project manager to connect all of these elements from within a small pharma company, communicating with five to ten different suppliers, co-ordinating work between them and ensuring they are communicating with each other. The model has something wrong with it," Geffroy says.



Formulation development scientist working on encapsulation technology for clinical batch manufacture at Almac

The Rapidd solution is based on (separately) sourcing both CMC requirements and non-clinical safety assessment and regulatory requirements from single teams on single sites. Almac brings in solid state services, radiolabelling, analytical development, chemistry and formulation capabilities, while a single CRO does the rest.

The groups at Almac and the CRO are thus linked, while also establishing a triangular model with the client, which takes charge only of project management. Almac will take charge of selecting and auditing the CRO, though the client can do as well if he wishes to. The key elements involved in a project are:

- API toxicology supply, including the first batch 10-50 grams, process R&D & the second, non-GMP batch of 100-500 grams
- GMP API supply, including solid state chemistry (salt, polymorph & co-crystal screen), scale up & 1-10 kg API synthesis
- Analytical method development & method validation
- Labelling, including stable isotope labelling & optional ¹⁴C radiolabelling
- Formulation to drug product, i.e. formulation development & drug product manufacture & release



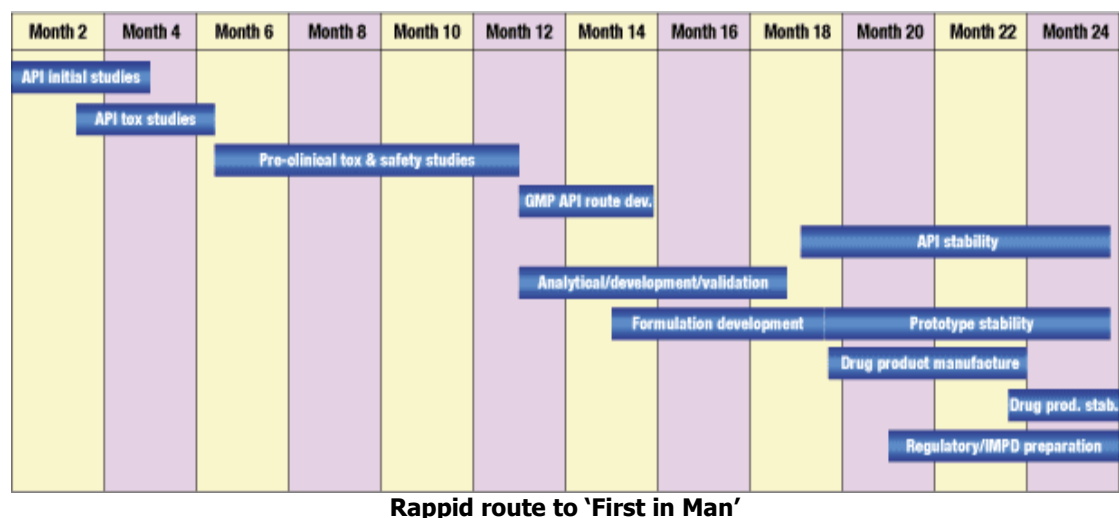
- ICH stability studies for the API & drug product
- Pre-clinical safety assessment, including genetic toxicology, safety pharmacology, bioanalysis and metabolism
- Regulatory support, including CMC documentation & CTA/IND submission

It appears straightforward but, says Geffroy, companies like Almac rarely talked to CROs before. This is, in large measure, what gives Rapidd its value.

Almac is now working in this way with three CROs. They have not been named yet but all are global top ten players, with operations in both the US and Europe. It has no plans to expand the network, because it regards having a limited number of close relationships as crucial to the success of the model.

Traditionally the route to first in man goes through a large number of stages that happen one by one, often with little or no overlap and a lot of time waiting around for results. This can take anything from 18 months to two years.

Rapidd changes this model by getting more done upfront. Figure 1 shows an archetypal process, though it could be far more complex in practice. One element is starting on API synthesis before doing the toxicology studies which, Geffroy admits, involves a calculated risk, balancing three months of time against potentially thousands of dollars in extra costs.



“As soon as a project team is in place, we sit down with the client,” Geffroy says. “Each has a different attitude to risk. Some clients are ready to go ahead with API synthesis upfront, some will prefer to wait until the tox study is done. The model has to be flexible – what we ask is what risks they are ready to take.”

If the decision to take a risk comes off, anything up to a year can be saved. This is ultimately down to the client to choose, guided by Almac’s experience. He will probably end up paying more per project but less overall.

“We can, for example, make 500 grams to one kilo of non-GMP material for tox studies. It doesn’t cost much more to do the non-GMP synthesis of the first three steps and make five to ten kilos straight away, so we can do that at the same time,” remarks Geffroy.



Typically, he adds, in the historic pattern, a client would ask us for a kilo of non-GMP API for toxicology studies to be carried out by a CRO, then scale-up the first choice synthesis route. Sometimes, this would lead to nasty surprises and end up costing more if, for example, the yield was too low.



Isotope chemistry lab, with yellow triangle badge to show that the company has the appropriate responsible person certification

“With the tox people sitting in from the start, you can work out more detail then,” Geffroy says. “It can be as basic as just finding out who has a few grams of material for contingencies. This can cut out a lot of double or even triple accounting – the CRO can say that you only need five kilos instead of ten, for example.”

Almac’s ability to develop this model is based in part on the general trend to specialisation. CROs and CMOs have largely retreated from the diversification into other fields that made them competitors. Now, they are more able to work together.

Simple though it sounds, the model may be unique. The only other company touting a package like this in the market at present is Aptuit, which launched its Indigo model at CPhI Worldwide 2008 in Frankfurt last year. However, this does not include API synthesis and toxicology is a relatively small part of the offer.

Where before Almac was essentially selling projects to scientists, Rapidd has brought it before another audience. “Now we are selling to a very different set of people – CEOs, CFOs, CSOs and venture capitalists, who can relate to the time-saving benefits,” says Geffroy.

Almac would always advise its small clients to keep their existing advisers if they take on Rapidd, in order to get the right perspectives on risks. Naturally, it assumed at the outset that these companies would be their sole market here, but Geffroy has talked with some Big Pharma companies too.

“Amazingly enough, they were quite receptive to it,” he says. “With hindsight, it is not that surprising since the three barriers of time, cost and attrition apply no less to them. Of course, they will not be such a good market because they have more capabilities in-house, not to mention their silo organisational structure. Small pharma firms are looking to outsource from the outset.”



Sir Allen McClay has signed part ownership of the Almac Group to a charitable trust

Almac is confident that this concept is ready for take off. In line with the market as a whole, pre-clinical and Phase I trials has been the hardest hit of its businesses in the downturn as so many early phase projects have been put on ice as companies focus their limited resources on shepherding their most promising candidates into Phases II and III. Even so, business is currently 11% up on 2008 levels.

"I believe that there is a backlog of projects waiting to go ahead into Phases II," says Geffroy. "Whether it will be in three, six or 12 months is something I don't know but Rapidd will help us to do better in the market of the future."