

GalChimia: supporting major pharma research projects

GalChimia is a Spanish CRO building a new campus next year that will quadruple lab space to meet current and future demand. In addition, the company recently concluded an agreement to support the collaboration between the three largest Spanish pharma, Almirall, Esteve and Palau Pharma, in osteoarthritis, by preparing standards and chemical series for the hit-to-lead and lead optimisation phases of the project.

Founded in 2001, GalChimia has become a leading synthetic organic chemistry company in Spain, providing custom synthesis, contract research, process development, reaction optimisation and analytical services. Over the past six years, the company has completed more than 500 projects in the drug discovery field and more than 30 process development projects. "One of the original ideas was to take all the expertise and experience in organic synthesis in academic research and apply it to synthesis projects in the pharmaceutical industry, that is, the synthesis of small molecules with therapeutic potential," says Dr Jacobo Cruces, the company's CSO. "We had a lot of success approaching problems with a synthetic organic chemistry mindset as opposed to the more conventional medicinal chemistry approach.

"Spain does not have a long tradition in entrepreneurship," he observes. "The levels of investment in biotech start-ups are lower compared to those in other countries, so funding is usually a problem for many

Spanish biotech companies. Additionally, most Spanish biotech companies are focused exclusively on the development of new products. Some of them try a mix of services and product development as a way to generate cash in the short term while pursuing new products in the long term.

"Our company, however, has never been focused on the development of a new product or technology," he states. "We are not a technology company. Our exclusive focus is the client: the client's needs in terms of deadlines, project goals, products and so on. So our aim is always to meet our client's expectations while generating new value, striving always to increase our contribution to the project. With this focus, ever since GalChimia was founded, we have incorporated the latest synthetic technologies, and we can now offer a broad range of techniques, including flow chemistry."

Contracts with large pharma

GalChimia began business with just one employee at the end of 2001 but by the end of

2002, the company had established long-term drug discovery contracts with the two largest Spanish pharmaceutical companies.

"We demonstrated that we could meet the deadlines and solve challenging synthetic problems," says Cruces. "Since then, we have started collaborations with companies throughout Europe and the USA, all under the usual service model. Very recently we started a partnership with Alfama, a Portuguese company now headquartered in the USA that has unique expertise in the development of carbon monoxide releasing molecules, or CORMs. We are also entering long-term collaborations with other companies, always contributing our skills in organic synthesis to the partnership.

"Though our growth has been uninterrupted since we started the company, we are reaching the limits of our current facilities. To answer our client's needs and keep ourselves at the cutting edge of organic synthesis, we need to increase our lab space so we can keep introducing new synthetic and analytical equipment into our labs. This will also allow us to offer our clients larger and more efficient work teams," he says.

Major arthritis research project

GalChimia is providing support to the Neogenius project, the main objective of which is the discovery and development of new medications for the treatment of arthritis. The company's role is to support the effort of the chemistry teams in the three companies participating in the project, Almirall, Esteve and Palau Pharma, by preparing chemical compounds ranging from standards to libraries of new molecules for the hit-to-lead and lead optimisation phases of the project.

The project has been designed to have a three-year duration with a budget of €15.4 million and includes the participation of several research organisations as well as small and medium-sized companies.

"We are used as a resource to cover targets that require the development of routes that are longer or more speculative than the usual



GalChimia approaches problematic synthesis projects with a synthetic organic chemistry mindset rather than a medicinal chemistry approach.

Case study 1: drug discovery

In one of its research collaborations, a biotech company contacted GalChimia to access its chemical services. The goals of the research were to generate intellectual property as fast as possible in two different projects where hits were available. In one project, the synthetic route that was being used was too long and unreliable, and not flexible enough to introduce diversity. For the other project, no route was available, only structures drawn on paper.

GalChimia put two people to work on each project, and for one-and-a-half years routes were scouted, tested and optimised. The

company generated, tested and improved upon compounds during the hit-to-lead stage, and, when a critical commercial raw material was scarce, the company developed a procedure to prepare it from inexpensive, readily available substances and a catalyst.

The results of the project were that four patents were generated, increasing the value of the biotech company. One of the projects reached the lead optimisation stage and larger quantities of specific compounds were required. The scale-up was performed by GalChimia and compounds were delivered in time for in-vivo assays.

chemistry sequences; that is, when it is perceived that a completely new and 'risky' chemistry must be developed to pursue a particular route," explains Cruces. "One of the most interesting points of the collaboration is that it allows the coverage of more biological targets and chemical space than the usual drug discovery project, with each partner sharing and contributing its expertise in this therapeutic area. The deadlines have been met, many different chemical series have been explored, and very soon the molecules to be further developed will be selected. Obviously we would like to be the company working on the selected candidate, but as usual biology will have the last word."

Expanded facilities, increased service offering

Cruces says GalChimia has very exciting growth plans for the near future:

"We work with most of the biotech companies in Spain, and we are looking forward to expanding our client base among the mid-size pharma and the biotech sector in Europe. Of course, increasing our lab space and team is a pivotal part of this strategy.

"The biotech sector offers great potential for us. Many biotechs have a deep knowledge of biology, but they lack not only chemistry capabilities, but also knowledge of medicinal chemistry. We currently have several

a 98.8% conversion in just six hours with a very low impurity profile.

The third stage was optimisation. GalChimia designed a two-level factorial with three variables: catalyst load, temperature and pressure. The nine experiments were run and the results analysed using Design-Ease software. The most significant parameter was catalyst loading. The combination of pressure and catalyst loading was found to be a secondary factor, but with much less effect. Temperature was the third factor. With low catalyst loading, its effect was higher at high pressure, but it had little overall effect. The Design-Ease software predicted that catalyst loading could be reduced if pressure, temperature and reaction time were increased. If lower loadings were required for scale-up, these options would be realistic, since the product did not decompose under the reaction conditions.

Case study 2: reaction optimisation in process development

In a second case study, one of GalChimia's clients approached the company regarding the optimisation of the reduction of a halogenated nitroheterocycle. The starting process used Raney nickel as its catalyst to yield 60% of product, plus several impurities.

GalChimia tackled the problem in three stages:

First, the company obtained more information about the starting material, mainly to find possible solvents for the reaction. The starting material was incompatible with nucleophilic solvents, and its solubility in other solvents commonly used in hydrogenation was also an issue.

Second, the company concentrated on the reaction. It screened catalysts, as some of the impurities arose from a competitive dehalogenation during hydrogenation of the nitro group, and discovered that a commercial platinum-based catalyst allowed

Meet the management of GalChimia



Dr Jacobo Cruces is the chief scientific officer of GalChimia. He and Dr Carme Pampin founded the company with two other private partners and the venture capital company Unirisco Galicia in 2001. Dr Cruces obtained his MSc in Organic Chemistry from the University of Santiago de Compostela in 1995, and obtained his PhD in 2000.

Dr Carme Pampin is the chief executive officer of GalChimia. She obtained her MSc in Organic Chemistry from the University of Santiago de Compostela in 1996, and obtained her PhD in 2001.

collaborations with biotech companies where we contribute not only our chemistry skills, but also experience in medicinal chemistry regulatory issues."

"In addition, our business line of analytical services was launched after receiving some enquiries from our clients regarding product stabilities and similar problems. Providing them not only with chemical compounds but a view of the medicinal chemistry field and working closely with them in their projects is very exciting and rewarding. In the end, the old adage about 'their success is our success' is really true.

"We have also been working for the past two years on the development of new reactions in the field of green chemistry, more specifically, the use of copper to carry out reactions that are currently performed using palladium. These reactions have great potential and we have published a couple of papers on them aimed at medicinal chemists, but more results will be published very soon. Although the work does not have commercial applications in its current form we are exploring some very promising venues," he concludes.

Further information

GalChimia
Cebreiro, s/n
15823 O Pino
A Coruña
Spain
Tel: +34 981 814 506
Fax: +34 981 814 507
Email info@galchimia.com
Web: www.galchimia.com