Integrating expertise for full hit-to-candidate services

Serge Petit, founder and CEO of Idealp-Pharma, describes how chemistry, cheminformatics, screening, early ADMET and preclinical development can be combined to speed up the hit-to-candidate process.

In June this year, Idealp-Pharma launched fully integrated drug discovery and preclinical development services combining medicinal chemistry, cheminformatics, screening, early ADMET and preclinical development capabilities to speed up its partners' and clients' small-molecule programmes from biological target to first-in-man use. Dr Serge Petit, the company's president and CEO, comments:

"Being a one-stop-shop company adds significant value because the lead optimisation process involves iterative cycles for incremental optimisation. The main advantages of our one-stop-shop service are to have access to all the experimental data, to be able to refocus the synthesis programme and then to make the best decision for the lead optimisation process in accordance with our customers' specifications.

"Idealp-Pharma manages its customers' hit discovery and validation, hit-to-lead progression and lead-to-candidate process. Our aim is to deliver chemically and biologically validated hits, accelerating lead optimisation and identifying IND candidates for our customers."

Idealp-Pharma was founded in 2000 by Petit and started by performing contract research chemistry for one of the large pharmaceutical companies. Following this successful collaboration, the company provided chemistry services for mid-sized pharma companies and for biotechnology companies.

"Our medicinal chemists are experienced in building SAR and optimising pharmacological properties with expertise in devising novel synthetic routes for molecules of interest in a broad range of therapeutic areas and compound classes," says Petit. "We have a particular expertise in steroid synthesis, boronic chemistry and carbohydrate chemistry. The Idealp-Pharma team has taken 20 products to Phase I during their aggregate 80 years of pharmaceutical research experience."

Idealp-Pharma also supports its clients' drug discovery activities by providing modular and customised services such as medicinal chemistry and cheminformatics studies:

"We identify and validate hits, optimise lead compounds and manage the lead-to-candidate process on the client's behalf. We can manage all the drug discovery process from the biological target to first-in-man use," says Petit. "Idealp-Pharma grants full Intellectual Property to its clients. The required project resources are measured in terms of FTEs and our clients are in direct contact with a dedicated project manager, a PhD, throughout the collaboration period. According to their small-molecule programme progression, the benefits for our clients are identification of chemically and biologically validated hits, acceleration of the lead optimisation process, and time-saving in preclinical development phases."

Identifying chemically and biologically validated hits

Idealp-Pharma designs focused and general drug-like libraries, starting from a highly diverse collection of commercial compounds. The company clusters, docks, screens and picks up hits for a target, on the basis of either a known pharmacophore or the active site's 3D structure.

"We perform the synthesis of selected chemical libraries using standard multistep and parallel synthesis and purification and analysis," says Petit. "We can assess a compound's activity in primary screening, including test design and set-up, evaluate chemical space and synthesise analogues for patent expansion and protection, measuring pKa values and assessing aqueous solubility and chemical stability. Our biology capabilities enable us to rapidly assess solubility in medium and culture buffers and generate an initial profile of a molecule's physical-chemical properties."

Accelerating the lead optimsation process

In each project, computational scientists, biologists and chemists work together in order to optimise the choice of building blocks, hit ranking, synthetic accessibility and SAR studies:

Meet Serge Petit of Idealp-Pharma

Serge Petit's career began at Hoechst (sanofi-aventis) in 1980 while he was still studying for a Masters in Organic Chemistry at the Claude Bernard University in Lyons, France. In 1986, he earned a PhD in Organic Chemistry from the same institution. He then joined the Centre International de Recherche et Technologies Avancées (CIRTA) and set up a medicinal chemistry department performing contract R&D for pharmaceutical and other companies. In 1988, he moved to ARD, where he set up and developed the company's chemistry department, which grew to a total of 25 staff. In 1994, he left ARD to found Ideal Sarl, a consulting firm specialising in industrial project management. This was followed in 2000 by the incorporation of a sister company, Idealp-Pharma SAS, dedicated to providing medicinal chemistry solutions.

"Our medicinal chemists are experienced in building SARs and optimising ADMET properties on the basis of primary and secondary screening results," says Petit. "Idealp-Pharma performs on-site, exploratory *in vitro* ADMET permeability assays, metabolic and plasma stability tests and CYP 450 inhibition and cytotoxicity tests on hits in order to give test compounds the best possible chances of being bioavailable *in vivo*. Raw experimental data are always available for discussion with our clients and synthesis programmes can be refocused at any time."

Identifying IND candidates

Idealp-Pharma's scientists can refine SARs against previously generated data and also following internal discussion with its biologists and computational chemists.

The company can also synthesise metabolites and monitor their activity. Drug selectivity and secondary target identification can be checked by inverse virtual screening. *In silico* ligand profiling helps address potency and selectivity issues and thus anticipates pharmacological side effects.

"Idealp-Pharma can manage its customers' preclinical development projects because drug discovery, optimisation and development are all linked," says Petit. "The *in vivo* bioavailability and toxicity of the most promising lead compounds can be assessed well upstream in the drug discovery process, in order to confirm previous *in vitro* ADMET results. We help our customers to complete their requirements for INDs and IMPDs with preliminary formulation, scale-up, toxicology studies, CMC, and safety, pharmacology and genotoxicity studies.

"In the second quarter of 2006, we launched exploratory *in vitro* ADMET capabilities that allow us to evolve from a stand-alone service in chemistry and medicinal chemistry to integrated drug discovery services," Petit continues. "We carry out on-site permeability assays (PAMPA), metabolic and plasmatic stability tests on human and murin microsomes, and cytotoxicity tests, including MTT, ATP or LDH release tests. All data and results from our chemistry, our computational approach, and our screening and ADMET tests are available for our clients and discussed by our team. The aim is to turn validated hits into candidates and then carry out *in vivo* evaluation."

Partnerships on a global service basis

Since 2007, Idealp-Pharma has had partnerships on a global service basis in drug discovery. The company has had partnerships with acknowledged specialists in early *in vivo* bioavailability and toxicity studies for the most promising lead compounds upstream in the drug discovery process in order to confirm previous *in vitro* ADMET results.

Marketplace trends

Petit says the highest demand is for a services company to offer innovation and new compounds and to cover all the stages of the drug discovery process because pharmaceutical companies and biotechs want to remain concentrated on their core activities:

"The global trends we see are that the pharmaceutical industry is looking for companies able to offer services with high added value. A lot of commercially available compounds have been screened by HTS techniques, and most of the original compound collections have been tested, so the challenge for contract discovery chemistry companies is in understanding precisely the biological issues of their clients' projects and to offer a focused approach fitted to these projects. Most of our clients are looking for compounds: hits, leads, candidates. With our biology, cheminformatics and preclinical capabilities, we are able to offer them compounds to validate hits, accelerate lead optimisation and identify candidates, thus enabling them to make the best decisions in their small-molecule programmes.

"To be competitive, discovery chemistry should not be considered alone, but should be integrated into a global preclinical process and be the link between sound science and therapeutic innovation. In order to achieve that purpose, companies must have a critical size and integrate all their capabilities and human resources in preclinical discovery and development," says Petit. "This also means that discovery chemistry needs to be linked to classical target validation and also to biological data like proteomics, biochemical pathways, and biomarkers. That's what Idealp-Pharma is doing and the company will reinforce this by upgrading its staffing in specialised capabilities and therapeutic areas and by increasing and optimising its medicinal chemistry capabilities. Chemists, biologists and computational chemists and biologists all work closely together to understand the target product profile and to offer to pharmaceutical companies and biotechs the best solutions for their small-molecule programmes. We choose to concentrate those capabilities and to implement our services and capabilities by internal growth because we think that scientists can work closely together if they can share their hypotheses, their inspiration and their ideas on one unique site." sp²

Idealp-Pharma: growing capabilities and services in drug discovery

Further information

Mehdi Chelbi
Business Development
Idealp-Pharma
66, boulevard Niels Bohr
Bâtiment CEI - BP 2132
F-69603 Villeurbanne cedex
France
Tel: +33 4 37 48 87 95
Fax: +33 4 78 93 56 53

Internet Links:

Email:m.chelbi@idealp.com
Web: www.idealp-pharma.com