Oncodesign S.A.

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# Macrocycle discovery complements a robust preclinical program

**Both a drug discovery company and a preclinical service provider, Oncodesign has combined its discovery and preclinical platforms while applying a unique and innovative translational research approach. The company is working within creative partnerships to drive development for oncology and other serious illnesses with no known effective treatment.**

Combining scientific expertise in medicinal chemistry, pharmacology and imaging with rigorous project management enables Oncodesign to create a continuum of service from a compound's conception to its clinical application. By maintaining a translational focus right from the start, the company can identify, as far upstream as possible, the therapeutic value of each molecule and its potential to become an effective drug for the right patient.

## A service partner for the long term

Founded in 1995 by Philippe Genne to discover new and effective approaches to treating cancer, Oncodesign Biotechnology was initially a pioneer in the preclinical assessment of anticancer therapies. Now a world leader with more than 3,000 therapeutic molecules tested, 500 clients and extensive preclinical drug development experience, Oncodesign has also developed a unique technology platform, Nanocyclix, designed to speed up the discovery of new oncology drugs and biomarkers.

The aim of Oncodesign's preclinical evaluation service is to maximize the value of a potential drug candidate. The team at Oncodesign generates as much information as possible about the pharmacological behavior of a molecule by designing a customized program from its three main areas of technological know-how—pharmacology (PREDICT), new predictive *in vivo* models (Chi-Mice), and state-of-the-art pharmaco-imaging (Pharmimage).

PREDICT employs *in vitro* and *in vivo* pharmacology for early proof-of-concept evaluation including: drug formulation for *in vivo* administration; pharmacokinetic profiling and pharmacodynamic biomarker identification; dose and schedule optimization; drug combinations; and drug efficacy and resistance evaluation. The Chi-Mice component focuses on the development of *in vivo* chimeric humanized models—from patient-derived xenografts to immunodeficient mice carrying a reconstituted human immune system—the most relevant of which can be designed for a tailored preclinical trial. Pharmimage involves multimodal, noninvasive pharmaco-imaging (single-photon emission computed tomography, magnetic resonance imaging and positron emission tomography) to determine clinically useful imaging biomarkers or assess the efficacy of anticancer compounds.

On the basis of these three platforms, Oncodesign offers a broad range of products and services for the assessment, validation, targeting and diagnostic linking of anticancer therapies. These enable potential treatments to be optimally positioned toward a disease indication and patient population. "We work with clients to select the most appropriate study design and screening method to conduct preclinical assays," said Genne, who currently serves as CEO. "Our experts in oncology work closely with our clients through all stages of the drug discovery and development process to provide a complete solution based on a wide range of integrated services."

A growing number of long-term contracts attests to the caliber of services offered by Oncodesign. In November, for example, Isarna Therapeutics chose for the third time to extend its experimentation services agreement with the company. Isarna is in search of therapeutics that fight cancer and effectively treat ophthalmic and fibrotic diseases. Less than a month earlier, Cellectis, a key player in immunotherapy and innovative therapies, secured Oncodesign's preclinical services for a further 18 months, continuing a preclinical collaboration first launched in 2013.

## Macrocyclic discovery

Since 2010, Oncodesign has incorporated its expertise in medicinal chemistry into the portfolio offered to clients. The Nanocyclix platform enables Oncodesign to design, synthesize and efficiently optimize new small molecule compounds for diagnostic or therapeutic use. Specifically, Nanocyclix produces potent kinase inhibitors that have unparalleled potency, selectivity and good drug-like properties.

Kinase inhibitors, a promising family of therapeutic molecules with an estimated market size of $38 billion, block the action of deregulated kinases, which are responsible for more than 400 diseases including many cancers. They account for almost a quarter of the pharmaceutical industry's R&D investments but have had mixed results.

What sets Oncodesign apart is that its Nanocyclix technology, based on a chemical macrocyclization process, permits the development of small but very specific and rigid macrocyclic molecules. This is owing to a three-dimensional shape precisely designed to inhibit the kinase responsible for a particular disease, including cancer, inflammatory disorders, autoimmune diseases and central nervous system disorders. "Our exclusive Nanocyclix technology makes it possible to design a new generation of kinase inhibitors that are more potent and more targeted than kinase inhibitors currently on the market, in order to limit side effects for patients," said Jan Hoflack, the company's CSO.

## Partnering

Nanocyclix can be applied to a partner's leads and targets or to those of Oncodesign: the company has used Nanocyclix to generate the Nanokinib library containing over 5,000 diversified and new kinase inhibitors. The knowledge-based library of kinase scaffolds and linkers provides highly potent and selective leads for well-established and unexplored kinases, substantially shortening the upstream research phases preceding clinical development.

Oncodesign is looking to collaborate on specific drug programs within its proprietary kinase discovery pipeline generated using Nanocyclix. Thanks to their tremendous potential, Oncodesign's molecules are already the subject of drug-discovery partnerships with some of the world's leading biopharmaceutical companies, including Sanofi, Ipsen and UCB.

"Our priority is to create and partner on strategic therapeutic and/or diagnostic research programs that bring significant value to patients," said Hoflack. "Through an integration of our four main complementary platforms, we are able to bring our partners a unique discovery approach from target to patient as part of a risk-sharing partnership."

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