

Oncodesign reports positive results for its MNK1/2 program

- MNK1 and MNK2 are kinases targeted in a major activation pathway for several cancers
- The program has identified highly targeted inhibitor molecules and produced promising cellular results paving the way for lead optimization to begin

Dijon, France, December 5, 2017 at 6:00pm – ONCODESIGN (ALONC – FR0011766229), a biopharmaceutical group specialized in precision medicine, is announcing that it has obtained positive results opening the way for the MNK1 and MNK2 (MNK1/2) kinase inhibitor discovery program to move on to the lead optimization phase.

MNK1 (MAP kinase-interacting serine/threonine kinase 1) and MNK2 (MAP kinase-interacting serine/threonine kinase 2) are kinases involved in the precocious gene transcription required for growth and the differentiation of normal cells. Inhibiting the MNK1 and MNK2 kinases curbs deregulation of eIF4e, a protein overexpressed in a large number of cancers and an indicator of a poor prognosis for patients. Their deregulation may lead to resistance to anti-cancer therapies via various mechanisms and diminished anti-tumoral immune response. Conversely, specific inhibitors of these targets could improve the efficacy of existing therapies. This Oncodesign program thus provides a promising line of research for new therapies against a large number of cancers, including head and neck, colon, breast and bladder cancer.

In the probe to lead phase, the MNK1/2 program produced positive results in a cell model expressing the relevant mechanism of action. That enabled Oncodesign to select two series of Nanocyclix molecules to commence lead optimization with a view to arriving at best-in-class drug candidates. As part of this phase, it will begin an exhaustive series of *in vitro* and *in vivo* biological tests, while in parallel conducting medicinal chemistry optimization of the inhibitor molecules already identified. The phase can take up to 36 months, and the success rate is typically around 50%. A medicinal chemistry team dedicated to the project will be set up within Oncodesign's research teams to implement this decision.

"Following on from the ALK1 program, MNK1/2 is the second to commence lead optimization in a very short period of time thanks to the expertise and additional resources invested in our drug discovery programs since we integrated the François Hyafil research center's capabilities", commented Jan Hoflack, Oncodesign's Chief Scientific Officer and Chief Operating Officer. "Selectively inhibiting MNK1/2 is an approach that dovetails perfectly with existing immunotherapies because it would provide new precision medicine solutions for patients with various different types of cancer."

"The beginning of this new phase illustrates the progress made by our portfolio of kinase inhibitors in oncology, with extremely promising applications as a combination therapy and against resistance to anti-cancer therapies. It provides another example of the potential of Nanocyclix technology to generate, very early on in the drug discovery process, molecules with promising properties for targets of interest that have been barely explored to date", added Philippe Genne, CEO and founder of Oncodesign. "Given the attrition rate specific to the lead optimization phase, we are pursuing several promising programs targeting various kinases at this point and intend to speed up the pace of our discoveries."

To date, Oncodesign's kinase inhibitor portfolio has 12 programs, including 4 in lead optimization (MNK1/2, ALK1, LRRK2, RIPK2) and a Phase 0/1 clinical trial (EGFR radiotracer), with first-in-human results anticipated by the end of the year.

About kinases and Nanocyclix[®] technology:

Kinases are a family of enzymes that play a key role in regulating most cell functions, such as proliferation, cell cycle progression, metabolism, survival/apoptosis, repair of damaged DNA, motility and response to the microenvironment.

Using its Nanocyclix[®] technology module, Oncodesign identifies macrocyclic molecules capable of inhibiting both known and unexplored kinases in a powerful and targeted manner. A large variety of kinase inhibitors are thus explored continuously, and only the most promising inhibitor/targeted kinase combinations are selected for more in-depth investigations.

Oncodesign has built a project portfolio with tremendous potential to treat diseases with very substantial unmet medical needs. This portfolio contains both molecules already at an advanced stage of clinical development (a PET tracer for a specific type of lung cancer) and molecules at an earlier stage of development.

About ONCODESIGN: www.oncodesign.com

Founded over 20 years ago by Dr Philippe Genne, the Company's CEO and Chairman, Oncodesign is a biopharma company dedicated to the precision medicine. With its unique experience acquired by working with more than 600 clients, including the world's largest pharmaceutical companies, along with its comprehensive technological platform combining state-of-the-art medicinal chemistry, pharmacology, regulated bioanalysis and medical imaging, Oncodesign is able to predict and identify, at a very early stage, each molecule's therapeutic usefulness and potential to become an effective drug. Applied to kinase inhibitors, which represent a market estimated at over \$46 billion in 2016 and accounting for almost 25% of the pharmaceutical industry's R&D expenditure, Oncodesign's technology has already enabled the targeting of several promising molecules with substantial therapeutic potential, in oncology and elsewhere, along with partnerships with pharmaceutical groups such as Bristol-Myers Squibb and UCB. Oncodesign is based in Dijon, France, in the heart of the town's university and hospital hub, and within the Paris-Saclay cluster, Oncodesign has 220 employees and subsidiaries in Canada and the USA.

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