OliX Pharmaceuticals
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Driving drug development through next-generation oligonucleotide technology

OliX Pharmaceuticals, the first Asian company to advance its own proprietary RNA interference (RNAi) technology platform into the clinic, is using RNAi technology to treat skin, eye and lung diseases.

Based in Suwon, near Seoul in South Korea, OliX Pharmaceuticals is a young biotech company with a grand mission: it aims to become one of the top three oligonucleotide therapeutics companies in the world, and the leading oligonucleotide therapeutics company focused on skin, ocular and pulmonary diseases, by 2020. OliX was founded in February 2010, supported by funding from both the Korean government and the Small Medium Business Administration, and it began work on its first program—the antihypertrophic scar therapeutic OLX101—in December 2011. Today the company has a full portfolio of pipeline products that locally target dermal, ophthalmic and pulmonary diseases, and is looking to partner on some of its candidates.

Meeting the delivery challenge

OliX's product-development pipeline is based on its cell-penetrating asymmetric small interfering RNA (cp-asiRNA) technology, which uses RNAi (**Fig. 1**). RNAi is a biological process by which siRNA molecules can 'silence' the production of a specific protein by cleaving the corresponding messenger RNA (mRNA). Because siRNA can target any human gene, and even act on exogenous genes derived from pathogens such as viruses, it can exploit so-called non-druggable targets that cannot be adequately reached by either small-molecule or antibody drugs. Moreover, because siRNAs act by preventing the production of disease-causing proteins, and small-molecule and antibody-based drugs act on disease-causing proteins that have already been expressed, the two approaches can be used in combination, with additive or even synergistic effects.

However, delivering siRNAs, which are bulky charged molecules, into cells can be a major challenge and requires the use of delivery technologies such as liposomes or nanoparticles, which may trigger unexpected adverse effects. OliX's cp-asiRNA molecules can enter cells spontaneously without complex delivery systems. This single-molecule approach for local applications means simpler manufacturing and fewer regulatory hurdles, which allows the company to create a larger pipeline of clinical candidates more quickly and at a lower development cost. OliX is able to move from a gene to five or six cp-asiRNA candidate molecules in as little as three to four months. And because OliX's proprietary asiRNA platform is more specific than conventional symmetric siRNA, it has fewer off-target and immune-related side effects.

Pushing through the pipeline

OLX101, which targets the connective tissue growth factor (*CTGF*) gene, is OliX's most advanced program, and is in clinical development as an intradermally injected treatment for hypertrophic and keloid scars. Existing treatment options for these types of scars are not based on the disease mechanism, and so have little efficacy or are associated with high recurrence rates. The Korean Food and Drug Administration approved OliX's investigational new drug (IND) application for OLX101 in January 2017, and a clinical-trial authorization application to the European Medicines Agency is planned for the second quarter of 2017. The right to develop and sell OLX101 in Asia has been licensed to the Korean company Hugel, and OliX is currently looking for global partners for development outside Asia.

A similar approach could be used for other fibrotic diseases. People with idiopathic pulmonary fibrosis (IPF) develop chronic and irreversible lung scarring. The disease is fatal, often within a few years of diagnosis, and there are currently no cost-effective therapeutics available. The cause of the disease is not clear, and with around 80,000–110,000 people with IPF in Europe alone, there is a clear unmet medical need. The drugs currently approved to treat IPF simply reduce the speed of lung-function decline, and show no effect on mortality in clinical trials. OliX is developing OLX201—the same molecule as OLX101—for IPF as an inhalable product that also targets the *CTGF* gene and is delivered locally to the lung. Local delivery reduces gastrointestinal effects, which are a common side effect of existing drugs. In mouse studies, OLX201 significantly reduced CTGF expression and lung fibrosis. This project is supported by a $1.8 million joint grant from A*STAR (Singapore) and the Korea Health Industry Development Institute. Clinical trials are planned for late 2018 in the United States, and OliX is looking for global partners, especially those with inhalable-formulation technologies, for further development.

In its ocular franchise, OliX's OLX301A is in development for both wet and dry age-related macular degeneration (AMD), which can both lead to vision loss. Dry or atrophic AMD is the most common form, and although it tends to worsen slowly, patients can develop geotrophic atrophy (GA) at the late stage of the disease. GA leads to severe vision loss, and no treatment options are currently available. Dry AMD can also progress to the wet form, in which vision loss is more rapid.

OLX301A targets a gene that is not directly involved in the VEGF pathway, and so could be a 'first-in-class' drug for wet AMD, with potential use in combination with anti-VEGF therapeutics or alone in those patients who do not respond to anti-VEGF agents. OLX301A could also become the first available treatment for GA, and has the potential to prevent the shift between dry and wet AMD. Studies of OLX301A in mice have shown a therapeutic effect similar to that of Genentech's Lucentis (ranibizumab) on wet AMD, and significant effects on dry AMD. Clinical trials in the United States could take place as soon as 2018, and OliX is now looking for global partners for further development, including those companies with noninvasive delivery technologies for retinal disease.

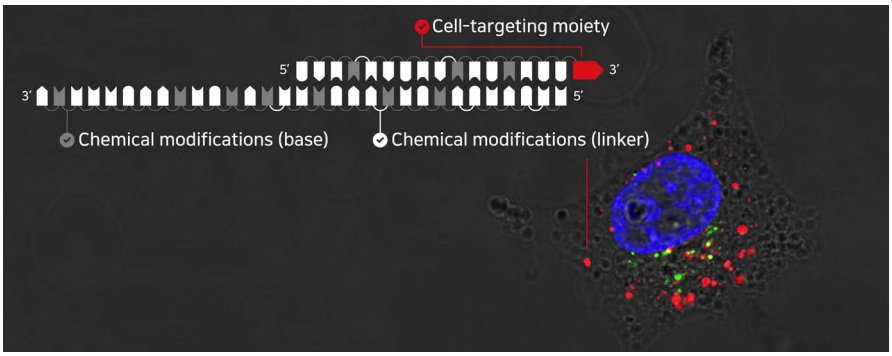

Figure 1: Cell-penetrating asymmetric siRNA (cp-asiRNA). cp-asiRNA is a chemically modified asymmetric siRNA that can be directly inserted into cells without a delivery vehicle to inhibit the production of disease-causing proteins.

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