



Exicure, Inc.
www.exicuretx.com

Harnessing the power of nucleic acids to treat cancer

Exicure is pioneering the development of spherical nucleic acid technology as a promising avenue of therapeutic development to strengthen and prolong the body's natural immune defenses against a wide range of cancers.

Cancer is a leading cause of mortality worldwide, accounting for approximately 13% of deaths each year. Despite recent advances in cancer treatments, a major challenge facing the field is the ability of many cancers to suppress the body's natural immune surveillance mechanisms that would recognize and destroy the cancer. Therefore, a key unmet medical need is a way to bolster the body's natural defenses to restore its immune surveillance capabilities in the context of a broad range of cancers.

Exicure is a clinical-stage biotechnology company pioneering the development of spherical nucleic acid (SNA) technology to mobilize the immune system to fight cancer. SNAs consist of densely packed, synthetic nucleic acid sequences radially arranged on the surface of a nanoparticle. The three-dimensional architecture of SNAs gives them important chemical and physical properties that strongly differentiate them from the traditional 'linear' forms of nucleic acids, enabling safe and effective delivery into cells and tissues (Fig. 1).

SNAs are attractive as novel therapeutics for cancer immunotherapy because they have a suite of useful properties leading to prolonged and multifaceted disease-fighting immune responses. SNA treatment could accompany other systemic therapies while driving a stronger immune response than other technologies.

"SNAs are revolutionizing the field of biomedicine by enabling powerful new tools that can be used to treat many diseases using DNA as a therapeutic molecule," said Exicure's CEO David Giljohann. "Exicure is building on the impressive work that has recently emerged in immunotherapy to create a powerful approach with SNAs working in conjunction with small molecules and antibodies for the treatment of cancer."

Stepping on the gas

Exicure's lead immunotherapy compound, AST-008, is an SNA consisting of oligonucleotides designed to activate Toll-like receptor 9 (TLR9) to drive a potent anticancer immune response. Throughout the early 2000s, linear forms of a TLR9 activator oligonucleotide

SNAs are revolutionizing DNA therapeutics with promising applications in immunotherapy

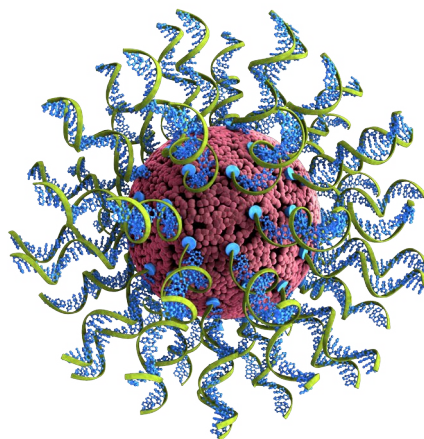


Figure 1: Structure of Exicure's spherical nucleic acid (SNA).

were tested extensively in clinical trials. These drugs were shown to be generally well tolerated but were not effective in producing an anti-tumor response. Since then, the advent of SNAs and checkpoint inhibitors has dramatically changed the therapeutic context for immune system agonists.

AST-008 produces a stronger innate immune response than conventional immunostimulatory oligonucleotides, enhancing the function and secretion of cytokines to a greater magnitude and for a longer period. Moreover, AST-008 promotes higher levels of antitumor activity than the historically used linear oligonucleotides.

Designed to fight many types of cancers, AST-008 shows promise both as a monotherapy and in combination with checkpoint inhibitors. Checkpoint inhibitors have been described as 'taking off the brakes' of the immune system, because they stop cancers from evading a patient's natural immunological antitumor activity. But for the majority of cancer patients with weak or highly suppressed immune systems, this strategy is only part of the answer. AST-008 provides the complementary piece by 'stepping on the gas' and upregulating the patient's immune system to attack the cancer now made visible with the checkpoint inhibitors.

To date, Exicure has demonstrated the remarkable ability of AST-008, either alone or in combination with checkpoint inhibitors, to reduce tumor volume and growth and increase survival in both prevention and established preclinical models of breast, melanoma, colorectal, bladder and lung cancer. With these promising results, AST-008 is expected to enter the clinic

in the first half of 2017. "In the end, this innovative immunotherapy approach could potentially offer patients both treatment for cancer and longer-term protection against recurrences, as well as fewer side effects than chemotherapeutics," Giljohann said.

Dramatic impact

Today, Exicure's pipeline includes AST-008, for cancer, and the gene regulation therapies, AST-005 and XCUR17, for dermatological diseases. Exicure is using its proprietary SNA technology platform to build a broad pipeline of products for a range of diseases with unmet medical needs. In addition to immunomodulatory drugs, the company is developing gene-silencing SNAs based on antisense molecules for therapeutic targets that are not amenable to small-molecule inhibitors or antibody-based drugs. SNAs based on these two classes of oligonucleotides hold promise for treating a range of hematological and solid cancers, inflammatory disorders and infectious disease.

SNAs are a flexible, scalable platform for drug development that can leverage almost any nucleic acid sequence or therapeutic modality. Whether it's a large or orphan indication, SNAs can stop disease at its genetic source. In addition, nucleic acid therapies promise to provide a far more economical path to drug discovery than other approaches, because the fundamental therapeutic oligonucleotide sequences can be determined and produced easily rather than through traditional techniques for chemical or protein synthesis, which are often highly complex and expensive. Leveraging state-of-the-art genomics, molecular biology and digital drug design, Exicure can go from target identification to clinical candidate identification in under 12 months at low cost.

To maximize the potential of its SNA technology platform, Exicure is seeking additional partnerships with pharmaceutical companies across multiple indications or within specific therapeutic areas. "Our first programs just scratch the surface of what we expect to be a growing pipeline of nucleic acid therapeutics," Giljohann said. "They will be the first demonstrations of a technology enabling our bold vision of making a dramatic impact on human health."

contact

David Giljohann, CEO
Exicure, Inc.
Skokie, Illinois, USA
Tel: +1-847-673-1700
Email: info@exicuretx.com