

CASE STUDY
AUGUST 2016

Aspyrian Therapeutics Inc.

www.aspyriantherapeutics.com

New Photoimmunotherapy redefines treatment of solid tumors

Aspyrian Therapeutics' new Photoimmunotherapy predicted to destroy tumors while activating immunological response

USA based clinical trials are underway for a new antibody anticancer platform, Photoimmunotherapy (PIT), a treatment showing promise in destroying tumors and activating immunological responses. PIT is expected to provide best-in-class therapies for solid tumors by both destroying the cancer cells and facilitating anticancer immune responses. PIT is highly tumor specific and can be used alone or in combination with other anticancer modalities to maximize therapeutic responses.

PIT was initially discovered at the US National Cancer Institute (NCI) by Dr. Hisataka Kobayashi and Dr. Peter Choyke. Aspyrian Therapeutics Inc. secured an exclusive license from the NCI to develop and commercialize PIT therapeutics. Aspyrian's main investor, Chairman and Director is Hiroshi Mikitani, the Founder and CEO of Rakuten Inc., a Japanese e-commerce powerhouse. Aspyrian's mission is to develop anticancer therapies with curative intent, and the current focus is to rapidly progress PIT therapies towards commercialization for cancers of high medical need.

The progress in developing PIT therapies has been very fast. Aspyrian began pre-clinical studies on its first drug, RM-1929, in October 2013. In July 2015, Aspyrian initiated a Phase I clinical trial to evaluate RM-1929 safety and anticancer activity in terminal head and neck cancer patients. Phase 2 studies began in June 2016 after submitting a new amended clinical protocol to the FDA (US Food and Drug Administration).

"PIT utilizes cancer-targeting antibodies conjugated with a non-toxic payload (IRDye 700DX) that can be activated at the tumor site with non-ionizing 690 nm red light," said Miguel Garcia-Guzman, Aspyrian's President and Chief Executive Officer. "Cell bound, light-activated conjugate induces cancer cell destruction without damaging normal tissues.

“Very rapid killing occurs within minutes, and is driven by biophysical disruption of cell membrane integrity. PIT only requires the antibody conjugate to bind tumors expressing the antigen,” said Dr. Garcia-Guzman.

Unlike classic Antibody Drug Conjugates (ADCs), cell-killing is neither dependent on antibody internalization nor on payload release.

Two different modalities

PIT can destroy locoregional cancers by targeting cancer cells directly but importantly PIT can also be used to enhance an immune response against the cancer so that the patient’s innate and adaptive immune becomes engaged to destroy both locoregional and disseminated cancers.

As described by Dr. Kobayashi, PIT-mediated destruction of cancer cells induces rapid Immunogenic Cell Death (ICD). Combination treatments of PIT with immune checkpoint inhibitors, such as anti-PD-1, anti-PD-L1 and anti-CTLA-4, are expected to enhance the immune response to cancer neoantigens.

In addition, PIT can be used as a new modality to activate directly immune oncological responses to the cancer. Thus, PIT based antibody conjugates can be designed to target and destroy infiltrating immune cells that create an immune suppressive or tumor promoting microenvironment. Killing immunosuppressive cells can facilitate adaptive immune responses against tumor neoantigens to both localized and disseminated tumors.

“The use of PIT to activate immune responses to the cancer is a new and exciting approach to engage the immune system of each patient against the tumor. This is a key priority for Aspyrian and we aim to validate this concept in the clinic as soon as possible” said Dr. Garcia-Guzman.

PIT initially targeting EGFR with RM-1929

RM-1929 targets EGFR, a cancer antigen expressed in multiple types of solid tumors, including head and neck squamous cell carcinomas (HNSCC). Aspyrian completed Phase 1 studies of RM-1929 in HNSCC terminal cancer patients who had failed all existing treatments including platinum-based therapies, and were not suitable for surgical resection or radiation therapy. Some had also failed Erbitux treatments (i.e. Cetuximab) or experimental drugs such as anti-PD-1 antibodies.

Phase 1 evaluated the safety and anticancer activity of a single treatment cycle, and defined the optimal RM-1929 dose infusion and light activation. Light, applied with lasers and fiber optics built to Aspyrian’s proprietary specifications, could be delivered to treat large multi-centimeter tumors at any location of the head and neck. Treatment was delivered in outpatient settings.

RM-1929 has progressed now into Phase 2 studies, which will evaluate long-term safety and efficacy of repeated treatment cycles in terminal HNSCC patients.

In early 2017, Aspyrian plans to conduct Phase 2 studies combining RM-1929 PIT treatments with immune checkpoint inhibitors such as anti-PD-1 antibodies. These studies will evaluate safety and synergistic effects of the combination treatment, and the sustained activation of anticancer immunological responses.

Pending outcomes of Phase 2 studies and regulatory agency approval, Aspyrian aims to initiate Phase 3 multinational trials in early 2018. Aspyrian aims to expand clinical development of RM-1929 to treat early stages of HNSCC, with the goal of setting a new standard of care for managing early and late stage head and neck cancer. Additional studies will test RM-1929 in other EGFR-expressing cancers.

Aspyrian also plans to advance new PIT therapies into clinical testing to expand its PIT pipeline. These products will explore both direct killing of cancer cells and uses of PIT to trigger an innate and adaptive immune response against cancer. The long-term objective is to optimize PIT therapies that can achieve both optimal control of locoregional disease and activate a durable immune oncological response, leading to complete cancer remission of disseminated disease.

“Aspyrian will develop RM-1929 and additional PIT products either on its own or by establishing strategic alliances for product co-development with partners. Aspyrian aims to be a long-term leader in oncology,” said Dr. Garcia-Guzman.