Aspyrian Therapeutics, Inc.
www.aspyriantherapeutics.com

aspyrian Therapeutics, Inc.

# Photoimmunotherapy redefines cancer therapy

**Aspyrian Therapeutics' Photoimmunotherapy destroys tumors while activating an immunological response.**

US-based clinical trials are under way for a new antibody anticancer platform called Photoimmunotherapy (PIT), which has shown promise in selectively destroying tumors and simultaneously activating an immunological response.

PIT was initially discovered at the US National Cancer Institute by Hisataka Kobayashi and Peter Choyke[1]. Aspyrian Therapeutics has secured an exclusive license from the institute to develop and commercialize PIT therapeutics. Aspyrian's main investor, chairman and director is Hiroshi Mikitani, the founder and CEO of Rakuten, 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 toward commercialization for cancers of high unmet medical need.

Aspyrian began preclinical studies on its first drug, RM-1929, in October 2013, and in July 2015 a phase 1 clinical trial was started to evaluate safety and anticancer activity in patients with terminal head and neck cancer. Phase 2 studies began in June 2016 after submission of a new amended clinical protocol to the US Food and Drug Administration.

"PIT utilizes tumor-targeting antibodies conjugated with a nontoxic payload (IRDye 700DX) that can be activated at the tumor site with nonionizing 690 nm red light," said Miguel Garcia-Guzman, Aspyrian's president and CEO. "The cell-bound, light-activated conjugates induce cancer cell destruction without damaging normal tissues."

Unlike with classic antibody–drug conjugates, PIT-mediated cell killing is not dependent on either antibody internalization or payload release.

## Two different modalities

PIT can destroy locoregional cancers by directly targeting cancer cells. Rapid cancer killing with PIT induces immunogenic cell death and releases cancer neoantigens, and could engage the patient's innate and adaptive immunity to augment the destruction of the locoregional tumor and metastatic cancer (**Fig. 1**). Combination treatments of PIT with immune-checkpoint inhibitors, such as anti–programmed cell death protein 1 (PD-1), anti–programmed death-ligand 1 (PD-L1) and anti–cytotoxic T lymphocyte–associated protein 4 (CTLA-4), are expected to enhance the immune response to cancer.

In addition, PIT can also be used as a new modality to directly activate immune responses to 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 with PIT can facilitate adaptive immune responses against the tumor.

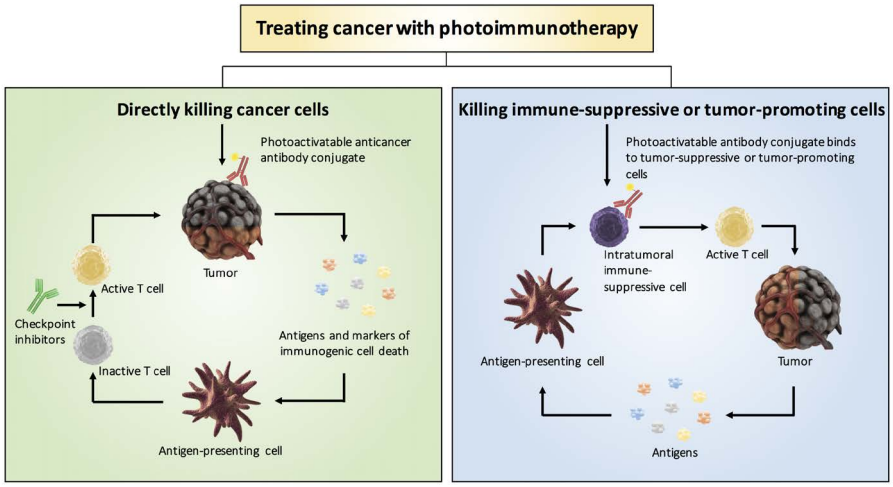


**Figure 1: Photoimmunotherapy can be used to kill cancer cells directly or activate an anticancer immune response by eliminating intratumoral immune-suppressive or tumor-promoting cells.**

"The use of PIT to activate the anticancer immune response opens the possibility for patients to generate an anticancer response against their own tumor. Aspyrian plans to validate this mechanism in the clinic as soon as possible," said Garcia-Guzman.

## PIT initially targeting EGFR with RM-1929

RM-1929 targets epidermal growth factor receptor (EGFR), a cancer antigen expressed in multiple types of solid tumors, including head and neck squamous cell carcinomas (HNSCCs). Aspyrian completed phase 1 studies of RM-1929 in patients with terminal HNSCC who had failed all existing treatments including platinum-based therapies and were not suitable for surgical resection or radiation therapy. Some had also failed treatment with Erbitux (cetuximab) or immune-checkpoint modulators such as anti-PD-1.

Phase 1 evaluated the safety and anticancer activity of a single treatment cycle and defined the optimal RM-1929 and light-activation dose. Light, applied with lasers and fiber optics, could be delivered to treat large (multi-centimeter) tumors at any location of the head and neck. RM-1929 has progressed now into phase 2 studies, which will evaluate the long-term safety and efficacy of repeated treatment cycles in patients with terminal HNSCC.

In early 2017, Aspyrian plans to conduct another phase 2 study combining RM-1929 PIT treatments with immune-checkpoint inhibitors such as anti-PD-1. These studies will evaluate safety and synergistic effects to sustain activation of the anticancer immune response.

Pending outcomes of phase 2 studies, Aspyrian aims to initiate phase 3 multinational trials in early 2018. The company will expand clinical development of RM-1929 to treat the early stages of HNSCC and will also test RM-1929 in other EGFR-expressing cancers.

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

"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 Garcia-Guzman.

1. Mitsunaga, M. *et al. Nat. Med.* **17**, 1685–1691 (2011).

contact
Miguel Garcia-Guzman, President and CEO
Aspyrian Therapeutics, Inc.
San Diego, California, USA
Tel: +1-858-925-5621
Email: miguel_guzman@aspyriantherapeutics.com