

# Mojave Therapeutics

Using Javelins to deliver disease-related antigens to immune cells

**H**eat-shock proteins (HSPs) are peptide-binding molecules known to refold proteins denatured by excessive heat. However, the immune system also uses HSPs to shuttle disease-related antigens to antigen-presenting cells (APCs), through which the human immune system can better “sense” invading pathogens or other rogue cells. Mojave Therapeutics is one of the most recent entrants into the HSP field, using these versatile proteins as the basis of novel therapeutics.

In many diseases, in particular cancer, the body fails to raise an appropriate immune response—specifically, cytotoxic T cells—against errant cells. Vaccines are therefore being developed as a means to kick-start this arm of the immune system to generate cancer-clearing T cells.

Timothy Cooke, Mojave’s chief executive officer, explains: “Traditional preventative vaccines stimulate the MHC [major histocompatibility] class 2 arm of the immune system, generating antibodies. But in order to treat disease using vaccines, you need to stimulate the [MHC] class 1 arm to get a good cytotoxic T-cell response.” Mojave seeks to harness HSPs’ natural role as antigen delivery vehicles to trigger specific cytotoxic T-cell responses.

Conveniently, HSPs deliver disease-related antigens directly to APCs, subsequently activating MHC class 1 immune reactions. Not all antigens bind effectively to HSPs, however. To circumvent this limitation, Mojave has designed a “one-size-fits-all” bimolecular linker, the “Javelin,” that works rather like molecular Velcro, according to Cooke. One end can bind strongly within the (constant) antigen-binding groove within an HSP, and the

other is variably modified to bind any disease-related antigen. The HSP–Javelin–antigen complex is then administered to the patient and taken up by his/her APCs, and the relevant T-cells are activated.

This cassette-like system, in which the Javelin can be used to link any antigen to

funds to last until mid 2003, and is currently evaluating the data from its phase 1/2 clinical trial for its first Javelin-based treatment, for melanoma. The company intends to grow to become a drug developer, retaining products in house for as long as possible before seeking partners.

Initially, the primary research focus will be cancer and chronic viral infections. “Our goal is to produce therapeutic vaccines [for cancers] as safe and as easy as a flu shot,” says Cooke. Two other companies also working with HSPs have products in clinical trials, providing some proof of

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an HSP, is patented intellectual property from the Memorial Sloan-Kettering Cancer Center (New York), where the technology originated. Cooke says that Mojave has no intention of becoming an antigen-discovery company. “The real bottleneck is in antigen delivery,” says Cooke, and so Mojave hopes to “do deals” with antigen specialists and capitalize on its strength in delivering those antigens.

For now, the company has sufficient

principle for the strategy: Antigenics (New York) uses HSP–antigen complexes isolated from a patient’s tumor, and StressGen (San Diego, CA) fuses the antigen to a mycobacterial HSP, creating a more rigid technology platform. Cooke says: “The field of HSPs is relatively young, but products are moving through clinical development and we will eventually be able to sort out which [approaches] are the best ones for a given disease target.”

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# Axxima Pharmaceuticals

Creating a firewall against infection

**W**hen pathogens infect a host, they must manipulate its signal-transduction pathways—the intracellular circuits that transmit extracellular signals from the cell’s surface to the nucleus, where cellular change can be realized—to survive. Axxima intends to prevent pathogens from hijacking these pathways by using inhibitors of kinases, enzymes that play key roles in cell signaling, to generate a “firewall” against infection.

Because disturbed kinase activity is known to lead to cellular malfunction, and thus to disease, kinases have become popular targets of drug development, especially in the areas of cancer, immunosuppression, and inflammation. Despite competition in this field, Axxima Pharmaceuticals was set up five years ago to develop small-molecule kinase inhibitors, which can block specifically those signal transduction pathways



Axxima’s Martinsried, Germany headquarters

involved in infectious disease.

What also distinguishes Axxima from the crowd, according to its chairman of the board Jürgen Drews, is that the company focuses its efforts not on kinases in pathogens (although it does some research in this area) but on kinases in the host.

**Founded:** February 1997

**Founders:** James Rothman, Frank Landsberger, and Ulrich Hartl

**CEO:** Timothy Cooke

**Employees:** ~30

**Financing to date:** \$24.5 million from Apax Partners (London), Johnson & Johnson Development Corporation (San Diego, CA), and Gobi Partners

**Location:** Hawthorne, NY

<http://www.mojave-therapeutics.com>