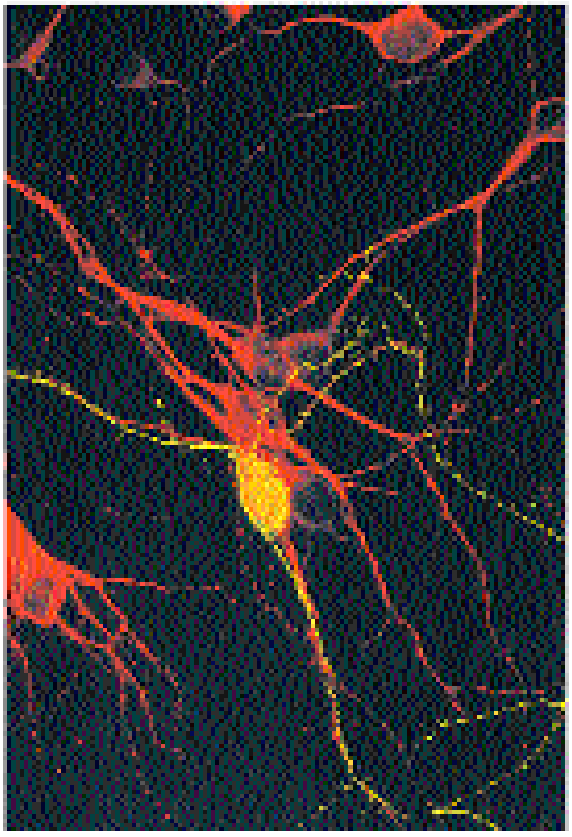
Advanced Targeting Systems



Yellow staining for saporin after internalization of
SP-SAP by this single spinal cord neuron in primary culture

Technology Summary

For Information Contact:
Denise Higgins, Vice President 858-642-1988

Technology Summary

Advanced Targeting Systems ("ATS") is a pioneer in the use of toxin conjugates targeted to eliminate specific cells through a powerful technique called Molecular Neurosurgery.

ATS is seeking an alliance to commercialize the therapeutic applications of Substance P-Saporin (SP-SAP), a large molecule, biochemical conjugate, that when delivered directly into the spinal fluid, seeks out and eliminates specific nerve cells that transmit chronic pain messages to the brain. Because of its size, this drug does not travel far from the site of administration. This has created great excitement in the scientific and medical communities.

This is an opportunity to participate in the development of a therapeutic with (1) **no drug discovery required,** (2) **patent protection,** (3) **successful preclinical data** (4) defined initial target market with **accelerated development** timeline, (5) **flexible partnering structure,** and (6) access to an established pipeline of **future targeting-based drugs**.

The FDA has suggested that the initial focus for SP-SAP treatment should be on the terminally ill cancer population. Of the 500,000 Americans who die of cancer annually, nearly 200,000 suffer horrible pain with no desirable alternatives. This treatment replaces drugs with unpleasant side effects and chemical/surgical methods that sever the spinal cord; SP-SAP only removes a few neurons. Management believes this market can generate over $300M annually, in the U.S. alone. Potential future opportunities include Rheumatoid Arthritis and Complex Regional Pain Syndrome ("CRPS"), both billion dollar markets.

Since 1994, Dr. Doug Lappi, the leading expert in the manufacture and use of targeted toxins, and his team at ATS have been developing and selling reagents to the research community and major pharmaceutical companies. In 1997, SP-SAP (a chemical conjugate of Substance P and the ribosome-inactivating protein saporin) was created to eliminate Substance P receptor (SPR) neurons that propagate the signal for chronic pain. ATS has successfully completed preclinical studies and initial safety tests in animal models, both funded by the National Institutes of Health, and was granted patent protection for SP-SAP in May of 2000 which covers all the various configurations for SP-SAP.

SP-SAP preclinical data were the basis for two articles in *Science* and received international press coverage. The mechanism of SP-SAP is well understood. It enters SPR-positive neurons by internalization of the ligand-receptor complex. SAP enters the cytoplasm and enzymatically inactivates the ribosomes and shuts down protein synthesis, resulting in cell death. Four key points from these results are: (i) SP-SAP **greatly reduces neuropathic and inflammatory pain**, (ii) **normal pain transmission is completely retained**, (iii) **pain relief appears permanent with no collateral pain states**, and (iv) **pain that occurs after treatment with SP-SAP can still be treated with morphine**. The FDA reviewed the data and this formed the basis for their instructions on the continuing development of the drug.

The chronic pain population is one of the most pressing healthcare issues in the world. Estimates for the size of the market range from 50-100M persons in the U.S. alone. Chronic pain is an extremely common affliction from migraine headaches, to fibromyalgia to terminally ill cancer patients. The pharmaceutical market for powerful, sustained-release painkillers for patients trying to manage chronic pain is estimated at $2.3B annually. Chronic pain disables more people than cancer or heart disease and costs the American public more than both diseases combined—estimated at upwards of $40B in medical expenses annually.

Advanced Targeting Systems is seeking an alliance with a pharmaceutical or biotechnology corporation. ATS desires to transfer SP-SAP into a working environment that can quickly and efficiently take the drug to human clinical trials and on to market. Animal toxicology studies are already underway, GMP protocols have been written and with the proper infrastructure SP-SAP could be in clinical trials in one year. **Income from sales of the drug would be possible in three years**. ATS is working with leading universities, has assembled a stellar advisory board, and industry-leading cancer clinicians are waiting to participate in clinical trials. The proper alliance would be beneficial not only to the corporations involved, but to the millions who suffer from chronic pain.

Advanced Targeting Systems, Inc., 11175-A Flintkote Avenue, San Diego, CA 92121 USA

Background

Advanced Targeting Systems (ATS) is a San Diego-based biotechnology company dedicated to providing quality targeting reagents for scientific research and pharmaceutical development. For the past twelve years, ATS has primarily focused on the development and sale of products for the Neuroscience research community. The Company's current product line includes targeted toxins, antibodies and custom conjugation services designed to assist scientists in the study of nervous system function, brain-related diseases and disorders.

The technology that provides the foundation for the Company's products has a broad spectrum of applications, not only in the field of Neuroscience, but in virtually every medical and pharmaceutical research field in practice today. ATS is continuing to develop and expand the existing product line through strategic scientific collaborations with top scientists throughout the world.

During the past six years, therapeutic applications have been identified for one of the conjugates produced by ATS; SP-SAP (Substance P-Saporin). Part of the corporate strategy is to form a strategic alliance to allow the transfer and development of these drug candidates.

ATS has had product sales from the very first year of business. This is a private company with no outside investors, funded by sales and SBIR grants.

Technology/Product Information (SP-SAP)

SP-SAP is a chronic pain therapeutic with a completely innovative and unique mechanism of action. The competition in the chronic pain market is broad, however, the FDA has suggested that the initial focus population be for terminal cancer patients refractory to opioid treatments, and the competition for this initial subpopulation is narrow. Once a patient is unresponsive to opioid treatment, there are few alternatives. Other than analgesics, options are limited to nerve blocks and unconventional treatments such as acupuncture or hypnosis. SP-SAP would be used when the patient's pain is not relieved by analgesics.

Revenue Potential

Estimates for the size of the chronic pain markets range anywhere from 50 million to 100 million persons in the U.S. alone. Chronic pain is an extremely common affliction that occurs in a variety of forms that include the specific pain of arthritis, the mysterious, all-over body pain of fibromyalgia, and the debilitating pain of the terminally ill cancer patient.

The pharmaceutical market for powerful, sustained-release painkillers that can be taken by cancer patients and others trying to manage chronic pain, is estimated at $2.3 billion annually.

Development Strategy

In order to achieve ATS goals for pharmaceutical development of drug candidates, it is necessary to fill in the expertise gaps lacking in the company. The strategy is to form an alliance with an organization with a track record in bring drugs to market, preferably with experience in the chronic pain market. ATS has in-house experience for research and development and will continue to produce candidates for the pipeline of therapeutics to be developed by a strategic partner.

SP-SAP Development History

ATS has invested over $3M in funding to the development of SP-SAP; from both SBIR and internal sources. This funding has accomplished the following thus far:

Patent Issued: U.S. Patent 6,063,758 was issued on May 16, 2000: "Substance P-Saporin (SP-SAP) conjugates and methods of use thereof." The claims in this patent cover all the various configurations for SP-SAP. There is currently a continuation in part (CIP) application before the patent examiner: U.S. Serial No. 08/890,157. This CIP will cover therapeutic applications of SP-SAP and will further strengthen the patent position.

Preclinical Studies Complete: Efficacy and specificity studies in the rat model have been completed and resulted in two publications in the prestigious journal *Science*. Safety studies in the dog were completed in 2003. In 2004, GLP toxicology studies in the rat were begun; the final report was completed in October 2006. Studies in primate are slated to begin in 2007. Both studies have been funded by a contract from the National Institute of Mental Health.

Independent Research: SP-SAP is sold as a research reagent to scientists throughout the world. Their independent studies have resulted in 34 publications that describe the use of SP-SAP in variety of applications, including the study of breathing, sexual function, and different types of pain.

GMP production: ATS has completed the preparation of SOP's for the production of SP-SAP and is currently working with Dr. Art Frankel's expert team on the optimization of the drug preparation.