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START-UP



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PROTEOTECH INC.

Novel targets for attacking Alzheimer's at all stages

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- **Contact:** Alan D. Snow, PhD, president & CSO
- **Industry:** Pharmaceuticals
- **Business:** Drugs for Alzheimer's and other amyloid diseases
- **Founded:** June 1996
- **Founder:** Alan D. Snow, PhD
- **Financing to date:** >\$3 million

Researchers may not have gotten to the root cause of Alzheimer's disease yet, but most agree that the beta-amyloid protein is one of the culprits responsible for the disease's destructive effects. Pathological deposits of a sticky type of beta-amyloid form plaques on the outside of brain cells, triggering an inflammatory reaction that kills them. Many pharmaceutical companies have therefore chosen the beta-amyloid protein as a target to arrest or prevent the progression of Alzheimer's disease. **Bristol Myers Squibb Co., Amgen Inc., SmithKline Beecham, Elan Corp. PLC**, and others, for example, hope to inhibit various forms of

secretase, an enzyme that acts upon a precursor to beta-amyloid, in order to prevent the build up of the noxious protein. Elan has also conducted studies on a promising vaccine that uses a form of the beta-amyloid protein itself to prevent the formation and to reduce pre-existing deposits of beta-amyloid plaque.

All hope to participate in a multi-billion dollar blockbuster opportunity, but also to offer a therapeutic option to more than 4 million sufferers in the US of a disease for which there is no cure, only symptomatic relief, in the form of cholinesterase inhibitors **Cognex (Warner-Lambert Co.)**, **Aricept (Pfizer Inc.)** and **Exelon (Novartis AG)**. These scant few FDA-approved drugs merely retard cognitive decline in sufferers of mild to moderate Alzheimer's disease by preventing the breakdown of neurotransmitter acetylcholinesterase.

Researchers at the **University of Washington** believe they have found a novel approach that interferes with the harmful formation of amyloid plaques, and have formed **ProteoTech Inc.** to develop the patent-pending technologies. The university granted a worldwide, exclusive license to its amyloid attacking technologies to the start-up in exchange for an equity stake.

ProteoTech has a portfolio of product and diagnostic candidates based on the relationship of specific proteoglycans, a group of complex carbohydrate containing-proteins that are ubiquitous in organs and tissues, to certain diseases, including Alzheimer's, Type II diabetes, as well as Down's syndrome, cancer, arthritis, atherosclerosis and AIDS.

Proteoglycans appear to play a role in the acceleration of amyloid fibril formation. ProteoTech researchers also believe that when a particular proteoglycan binds to beta-amyloid protein, it protects the protein from protease degradation. Inhibiting the proteoglycan, therefore, will not only prevent beta-amyloid plaque formation, but will also clear out existing deposits, giving ProteoTech product candidates for the completely unserved sufferers of severe Alzheimer's disease. Since some of these compounds are also anti-oxidants and anti-inflammatories, ProteoTech's compounds represent a multi-target approach to disease intervention.

ProteoTech has six leads in preclinical development for Alzheimer's disease and Type II diabetes. One of its leads, PTI-00703 is a proprietary extract from the tropical plant, *Uncaria tomentosa* (i.e. Cat's claw). In labora-

tory tests, PTI-00703 prevented the formation and disrupted beta-amyloid deposits in the brain both in the test-tube and in animal models. ProteoTech has licensed dietary supplement uses of the compound to **Rexall Sundown Inc.** under an agreement that will provide it early revenues. Rexall Sundown launched three nutraceuticals covered by the agreement in 1999: *Neurosharp*, *Cat's Claw Complex* and *CognoBlend*; and the partners are currently conducting a one-year Phase I/II clinical trial at the Aging and Alzheimer's Center at **Oregon Health Sciences University** to test the efficacy of PTI-00703 on patients with mild to moderate Alzheimer's disease.

However, the company's principal focus is on prescription pharmaceutical products, to which it retains rights. Based on the active ingredients within PTI-00703, ProteoTech is developing PTI-777, a drug that aims to clear out accumulated beta-amyloid protein fibrils. The company therefore hopes to be in a position to target every stage of Alzheimer's disease from mild to severe. Cat's Claw extract appears to have more than one active ingredient, according to ProteoTech's scientific founder and president Alan D. Snow, PhD. "The mixture is very potent," says Snow, "but we plan to go forward with

the best active ingredient, a single compound that is synthesizable." Furthermore, there is now preliminary evidence that PTI-777 crosses the blood brain barrier, Snow claims, a bioavailability hurdle that stumps many developers of CNS drugs. In addition to the plant-derived product, the company's pre-clinical portfolio includes small peptides and carbohydrate mimics.

Snow believes the company's proteoglycan platform will provide other useful tools for Alzheimer's research. Particular proteoglycans may serve as diagnostic markers for Alzheimer's disease. And the company has developed proprietary animal model systems of Alzheimer's disease that are not transgenic, unlike the models of Novartis AG or Elan, so they don't take several months of breeding time to create. The company has found a way to insert and perpetuate amyloid in the brains of rodents.

In addition, ProteoTech plans to tackle the pathogenetic roles of proteoglycans in other human diseases including Type II diabetes and cancer, and will be actively looking for pharmaceutical partners in these areas.

ProteoTech plans to conduct Phase I and Phase II clinical trials itself before partnering. It aims to be in the clinic with PTI-777, a single ingredient de-

rived from PTI-777, in the next 12 months. Snow, formerly a Research Associate Professor of Pathology at the University of Washington School of Medicine, is currently president of the company as well as chief scientific officer, but the company will be searching for a CEO in the next year or two, Snow says.

Snow is a pioneer in the field of proteoglycans in Alzheimer's disease and other amyloid diseases, and has made important contributions over the years in this area of research. Gerardo Castillo, PhD, director of biochemistry, is a founding scientist of ProteoTech. Castillo worked in Snow's laboratory at the University of Washington for several years before joining the company. Dennis McCurley is ProteoTech's COO & CFO and joined the company last year after 20 years of senior management experience in the financial and retail distribution industries.

To date, the company has received more than \$3 million in funding from a combination of SBIR grants provided by the **National Institutes of Health** and individual investors. The company is currently raising another \$2.5 million in a Preferred Series private placement, and plans to raise additional funds once its other Alzheimer's drugs enter human clinical trials.



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