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# THE WALL STREET TRANSCRIPT

Questioning Market Leaders For Long Term Investors

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**THE WALL STREET TRANSCRIPT**

**CEO INTERVIEW  
WITH INVESTORS BRIEF**

**PAUL E. FREIMAN**  
Neurobiological Technologies, Inc.

# Neurobiological Technologies, Inc. (NTII)



**PAUL E. FREIMAN**, 64, joined Neurobiological Technologies, Inc. as a director in March 1997, and was elected President and Chief Executive Officer in May 1997. Before joining NTI, he was the former Chairman and Chief Executive Officer of Syntex Corporation, a \$2 billion pharmaceutical company. He was instrumental in the sale of Syntex to Roche holdings for \$5.3 billion. Mr. Freiman had a long and illustrious career at Syntex and is credited with much of the marketing success of Syntex' lead product Naprosyn®. He was also responsible for the move of Naproxen® to over-the-counter status, marketed by Procter & Gamble, as Aleve®. Mr. Freiman held a series of key positions both domestically and internationally, including president of the U.S. subsidiary, president and chief

operating officer of Syntex Corporation, and ultimately chief executive officer. He actively participates in pharmaceutical industry associations. He is former chairman of the Pharmaceutical Manufacturers Association and was a member of its executive committee and board of directors. He was the chairman of the task force to review the code of pharmaceutical marketing practices for the International federation of Pharmaceutical Manufacturers Association from 1991 to 1993. He served as a member of the Jackson Hole Group, a think tank in the field of health care reform for the United States. He also served on the board and executive committee of the Pharmaceutical Partners for Better Health Care, a global organization of CEO's of research-based pharmaceutical companies. Mr. Freiman is currently serving as chairman of the board of Digital Gene Technologies, a private genomics company, and serves on the boards of Penwest Corp., Calypte Biomedical, Otsuka America Pharmaceutical, Inc., and several biotechnology companies. He is an advisor to Burrill & Company, a San Francisco merchant bank. Mr. Freiman is the former chair of the University of California San Francisco (UCSF) Foundation and is a trustee of the Sacred Heart Schools of San Francisco. He has served on numerous charitable and non-profit organizations. Mr. Freiman graduated from Fordham University with a Bachelor of Science degree in Pharmacy. Following graduation he served in the United States Navy. He was granted an honorary Doctorate from the Arnold and Marie Schwartz College of Pharmacy and received the first "Friend of the Academy of Students of Pharmacy" award from the American Pharmaceutical Association. In 1991, he received the Award of Distinction from the Pharmacists Planning Service Institute.

## Company Description

**(GAA613)(12945)TWST: Please give us a brief overview of the history and your activities.**

**Mr. Freiman:** The company was founded in 1987 by a group of scientists supported by a local financier. The neuroscientists felt that many great drugs were being developed at the university level, but they weren't being commercialized. Their dream was to form a virtual company, before the term became popular, and with their connections they attempted to license-in products to the company. So if you looked at the pipeline, the R&D piece would not be part of the company's presence. We would license products in, we would develop them internally and then license them out to major pharmaceutical companies. Indeed,

the company licensed in four compounds from outside and over the

period of 11 years, have tortuously developed what amounts to two compounds. One of these projects is in Phase III and the other one is in Phase II right now. The company is very small. There are 10 employees at the moment. I joined the company as CEO after being asked to join the board in 1997. At that time there was a real need for business focus as opposed to scientific focus. With the years I spent in this industry as a CEO of a fairly large company, what we've done is cut the company's burn rate down substantially, moved the products through the clinical pipeline fairly rapidly and have struck a deal with a mid-sized German company, Merz +

Co. GmbH & Co., a Frankfurt-based company, to keep us going.

## Highlights

*Neurobiological Technologies is an emerging drug development company focused on the clinical evaluation and regulatory approval of neuroscience drugs. The company's strategy is to develop early-stage drug products, oversee clinical trials, and seek partnerships with other companies for late-stage development and marketing. CEO Paul E. Freiman discusses the development stages of the company's main drug products, forecasting commercialization in the year 2000 in Europe, and a year or two later in the U.S.*

A product by the name of Memantine was synthesized by a group of German scientists back in the '70s and the product appeared to have activity in the brain. It was marketed for use in Parkinson's disease, but its actual affect on Parkinsonism is mild. The product was approved by the German government and sold in Germany, Switzerland and Austria. A very good side-effect profile was developed in real-time use. But, they were getting anecdotal reports. Patients with dementia, who also had Parkinsonism, were responding well on the dementia side, but not so well in Parkinsonism. So they decided to change course and try and develop the drug for senile dementia, which really, in various stages, leads up to Alzheimer's disease. Now, the product that was discovered in the '70s, its composition of matter patent expired in 1994. So Merz took out a use patent on senile dementia at about that time. At the same time some researchers up at Harvard at the Children's Hospital were looking at this class of compounds which are called NMDA receptor inhibitors for a potential use in a variety of conditions, such as stroke, or neuropathic pain and AIDS-related dementia. In their research they found that this compound, which was now freely available to the public, was an exciting compound from the standpoint of activity. In Harvard, at Children's Hospital, they decided to take out a patent on the compound for AIDS-related dementia and for neuropathic pain. So now, if you can, picture two companies developing the same drug on parallel paths in different indications. Furthermore, Children's Hospital went ahead and speculated that the drug might work in glaucoma. They licensed the product for use in the eye to the Allergan Company, which is the largest ophthalmic company in the world. Now you have three parallel tracks. I became involved in 1997 and found out about this and thought it would be good to form a strategic alliance, at least with Merz. After a year, we formed a relationship whereby Merz and NTI are looking for a global marketing partner and, we're getting close. The only exception is Japan where Suntory, the major liquor distiller that also has a pharmaceutical arm, already has rights for that through Merz. Merz and NTI® will share the income proportionately that will be received from any deal that's signed with a major pharmaceutical company. That income is: NTI® will have rights to a small percentage of the sales for Alzheimer's disease and Merz will have rights for a minor percentage of sales in neuropathic pain and AIDS-related dementia, and Children's Hospital benefits through a stream of licensing fees that they'll receive. So, frankly, it's one of the most complicated and interesting deals I've ever been involved in. Now, we're seeking a fourth party to become the corporate marketeer. So, it's working.

**TWST: Can you give us an idea of the size and growth potential of your industry and the markets you'll be serving?**

**Mr. Freiman:** The product for Alzheimer's is infinite. In the sense that with a global population that's aging very rapidly, you are talking about tens of millions of patients that are going to suffer from that disease and there is no satisfactory treatment, as you know. There's one drug that Pfizer is selling in the U.S. which has

a mild impact, but it's what's available today. So I believe that any product that works would have the potential of \$500 million to \$1 billion in sales. The underscored words are "if the drug works," and that's why NTI® and Merz are doing clinical trials.

In terms of diabetic neuropathy (this is the condition that was thought to be important to the folks at Children's Hospital), in the United States alone, there are 800,000 patients with the affliction and it's a very, very painful disease that is not treated by normal analgesics. In fact, one of the treatments of choice today are a group of drugs called tricyclic antidepressants. We have a drug in Phase II clinical trials that appears to have some activity and we're now in a massive, 375-patient Phase IIB trial that will really prove whether the drug works or not in the condition. The potential with 800,000 patients in the U.S., and figure about three times as many on a global basis, you are looking at a product that has the potential of probably \$150 to \$300 million in sales, and growing, because the diabetic market is growing with the aging population. AIDS-related dementia is the other area we're involved in. This is really interesting, because with the new treatments for AIDS, patients are living a long time. And rather than being a fatal disease, we're looking at it as a chronic disease. As the patients are living longer, certain conditions are popping out, one of them being dementia. Dementia for an AIDS patient could involve motor disfunction (where movements are exaggerated or difficult), forgetfulness and depression. It's getting to be quite serious. I don't have a good handle of what the size of that market is because we've seen numbers that range from 5-22 percent of AIDS patients who get this condition. In a small company, I don't have the capacity, frankly, to go out and do major marketing research projects, so we're working closely with the AIDS community. In fact, there's a group within the National Institutes of Health called the AIDS Clinical Trial Group, that's ACTG. They are performing the trial for us and we're tied in with a number of AIDS organizations in that process. And we're kind of enthused about it.

To summarize the status of these products: I mentioned neuropathic pain is in Phase IIB trials and AIDS dementia is in Phase II trials. In the senile dementia or Alzheimer's, Merz has completed one major clinical trial with positive results, which they recorded at an international conference on Alzheimer's disease last July. So they finished one Phase III trial, they have two other major Phase III trials going in Europe which will end this Spring and they've initiated a U.S. Phase III trial. So in many ways, this little company of ours is now involved in a Phase III product, both directly and indirectly. And, if you look at the 2,200 biotech companies worldwide, there are only a handful that have had products that have reached that stage. So frankly, we're feeling pretty chipper about the prospect with this product.

**TWST: What is your time table? When do you think the products will be commercialized?**

**Mr. Freiman:** I think we will start seeing commercialization in the year 2000 in Europe and probably 2001 to

2002 to in the United States. The AIDS dementia product might receive early approval because of the criticality of the symptom. Then we have a second product that we're developing which chemically is called Corticotropin-Releasing Factor (CRF), and we've given it a trademark called XERECEPT™. The product has shown over the years the ability to reduce edema (swelling) and we have a Phase II clinical trial that is being undertaken now for what's called peritumoral brain edema. Essentially what that is, if you have a tumor on the brain, swelling results from that tumor. There's fluid that's exuded from your blood vessels; the cranium is a closed vessel and water has no place to go. Standard treatment today, has been with only one drug, Prednisone, which is a cortisone, a steroid. It is very harmful if taken over a long period of time. So our hope is to prove that our product works as well as the steroid and that it doesn't have the same side effects. NTI® has received orphan drug status for XERECEPT™ by the FDA. This means that this is a relatively rare condition, not like arthritis, and NTI® will be provided 7 years patent exclusivity after the drug is approved by the FDA. We think this is a product that has yet to prove itself. It has a long way to go. Nonetheless, it shows a lot of promise and we're forging ahead with it. So those are the two compounds that we're left with of the four that we licensed in.

**TWST: I've got a question on the limitations on growth for your company, I guess capital is one thing. Any other bottlenecks or roadblocks ahead?**

**Mr. Freiman:** It's really a cash-driven business and I think one of the things that shocks investors in biotechnology is the amount of cash that's used in developing drugs and the time that's spent. I'm not sure people sold the story well in the beginning. It still takes about 10 to 12 years to develop a drug. You get a lot of dry holes before you hit oil. Our company, over the past 11 years, has spent about \$33 million, which is a small number in this industry. Most companies that have products in Phase III have gotten into the hundreds of millions of dollars. And we've done pretty well, which may prove that the model that we set up initially is working.

#### Management

**TWST: How is your management team doing? Is it equipped to handle your growth strategy? Any areas you feel really outstanding among management or any areas that might need some shoring up?**

**Mr. Freiman:** Again, we are a very small company and we have very few managers; they are all worker bees. We have an excellent medical director by the name of Dr. Lisa Carr who worked with me at Syntex. She's critical in terms of overseeing the clinical trial program. Her chief person, Erica von Studnitz, is a very experienced clinical research manager who is also working with Quintiles. Quintiles is a CRO and handles the trials for us. NTI® is providing the oversight and knowledge to that trial program. And, we have an experienced administrative head named Calvert Yee. Essentially I've been in this business since I was born, almost in the

back of a pharmacy in New York. I've been in the pharmaceutical industry for about 40 years and I grew up with Syntex and ended up as CEO and chairman. Syntex was a lot more complicated than NTI®. So, frankly, I don't see the management as an issue. We have a clear-cut mission to develop Memantine and CRF and get it to the market quickly. Our only constraints are capital, not management.

**TWST: Do you have a CFO or financial officer?**

**Mr. Freiman:** No, our CFO left and I am kind of chief cook and bottle washer. Since there's no money coming in, it's pretty easy to count it going out. So we have a very fine accountant who is working for us while Ernst & Young, our auditors, have been a lot of help.

**TWST: Do you offer stock options or perks to your people?**

**Mr. Freiman:** Absolutely!

**TWST: Does everybody get stock options?**

**Mr. Freiman:** Everybody is a potentially wealthy person if the stock comes through. But the stock has taken a terrible bath over the last three or four years. I personally believe if we can put a plug in it, it's really an undervalued stock. On the basis of having a drug this far along in development, of having no debt at the moment and a low burn rate (we are really husbanding the cash like Scrooge), I think the company has potential to make some money for our shareholders.

**TWST: What are your basic business principles or your management philosophy? What are the underlying themes you rely on to set the goals and the course of conduct for Neurobiological Technologies?**

**Mr. Freiman:** My answer could be generic for the biotech industry, but the two principles that are the most important are one, that cash is king. Everyone has to understand that we're working with other people's money and that every penny we spend is a penny that we don't have to spend tomorrow. So, the cash side of the biotech industry in our company is critical. The second thing is focus. When I joined the company a year and a half ago we had three products in development and all were being developed. I guess, on parallel tracks, a little bit here, a little bit there, and a little bit there in terms of spending money. What we've done is, if you can picture three railroad tracks, and take three trains and put them on one track. There's the first, second and third car. I decided to let one of the cars (products) go. So we now have two cars (products), clearly one in front of the other and everybody focuses in on that. As far as my management philosophy – hire good people, motivate them both with kindness and with stock options, but also set goals everyone has to hit. We're running a company of 10 people, instead of the 15,000 that I used to run, which is not very hard. In fact, it's a pleasure, because you walk around the office and get the message to everyone every day. It's not a difficult management chore.

**TWST: Looking at your financial reports, what are a couple of items or statistics that would give a long-term investor greater insight into your company?**

**Mr. Freiman:** I think since there is no income at the moment, we're looking at burn rates. When I joined the company we had a burn rate of \$800,000 a month. We're down to about \$300,000 a month and, with the ongoing clinical trials, we may get up to \$400,000 a month, but that's it. The prospect I see for the company is to receive multimillions of dollars of income through the arrangement with Merz, and when the burn rate reverts back to under \$300,000 a month (possibly lower), NTI<sup>®</sup> could be a cash machine if our products truly meet their place in the marketplace.

**TWST: Is there anything we've overlooked?**

**Mr. Freiman:** It's such a basic business – we make the products and we try and sell them. The biggest obstacle we have is the lack of cash. We're constantly out there trying to raise funds – the same as most every other biotechnology company. As you know, microcaps in our industry are in disfavor at the moment. So, the

chore is not easy. But, I think the products have been good enough to warrant the attention that we're giving them and we're going to raise the cash. □

**TWST: Thank you.**

**PAULE. FREIMAN**

**President & CEO**

**Neurobiological Technologies, Inc.**

**1387 Marina Way South**

**Richmond, CA 94804**

**510-215-8000**

**510-215-8100 - Fax**

*Each Executive who is the featured subject of a TWST Interview is offered the opportunity to include an Investors Brief or other highlight material to be provided and sponsored by and for the company. This Interview with Paul E. Freiman, President & CEO of Neurobiological Technologies, Inc. is accompanied by an Investors Brief containing corporate information.*

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# Investors Brief



**Neurobiological  
Technologies, Inc.**

Ticker (exchange)  
Price close 2/10/99  
12 Months Price Range

NTII (OTC BB)  
9/16  
3/8 - 1 3/4

## Corporate Headquarters

1387 Marina Way South  
Richmond, CA94804

Phone: (510) 215 8000

Fax: (510) 215 8100

Web: www.ntii.com

## Investor Relations Contact

Paul E. Freiman

## Corporate Officers

**Paul E. Freiman**

President and CEO

**Lisa U. Carr, M.D., Ph.D.**

Director of Medical Affairs

**Calvert Y. Yee**

Vice President, Operations  
and Administration

## Corporate Business Description

NTI<sup>®</sup> is an emerging drug development company focused on the clinical evaluation and regulatory approval of neuroscience drugs. The company's strategy is to in-license and develop early-stage drug candidates, oversee the human clinical trials to establish preliminary evidence of efficacy and seek partnerships with pharmaceutical and biotechnology companies for late-stage development and marketing.

NTI<sup>®</sup> is currently developing two product candidates in Phase II clinical trials. The company is developing Memantine, which appears to restore the function of impaired neurons by modulation activity of the NMDA receptor, integral to the membranes of such cells. Such restoration of function may inhibit injured or damaged neurons from firing abnormally, a pathological process associated with many neurological conditions, including dementia, Alzheimer's disease, neuropathic pain, and AIDS dementia as a potential neuroprotective agent. XERECEPT<sup>™</sup> is being developed as an anti-edema agent, for peritumoral brain edema (swelling of the brain caused by a tumor). XERECEPT has been granted orphan drug designation by the FDA. NTI<sup>®</sup> is seeking to out-license Dynorphin A, a human peptide previously tested as an analgesic agent.

## LARGE CLINICAL NEED

Treatments for many serious neurological disorders either do not exist or are limited by serious side effects. Common pathways of neuronal injury lead to functional impairment in many disorders, including AIDS dementia, diabetic neuropathy and brain cancer.

## COMPOUNDS IN DEVELOPMENT

**MEMANTINE:** An NMDA receptor antagonist that can be delivered orally and which appears to work by interrupting

a cascade of events resulting in neuronal death. By preventing the toxic influx of calcium into nerve cells, Memantine may reduce the likelihood of progressive brain damage and neuropathy. NTI<sup>®</sup> is developing Memantine in cooperation with Merz + Co. GmbH & Co. of Frankfurt, Germany.

**XERECEPT<sup>™</sup>:** A natural human peptide which may reduce brain swelling due to brain tumors. By halting the flow of fluids into brain tissue, XERECEPT<sup>™</sup> may prevent the build-up of pressure within the confines of the skull. NTI<sup>®</sup> is currently conducting a Phase II trial to evaluate the ability of XERECEPT<sup>™</sup> to control neurological symptoms of brain swelling.

## PAINFUL DIABETIC NEUROPATHY

**DESCRIPTION:** Chronic unrelenting pain which arises when a diabetic patient's nerves are damaged. Damaged peripheral nerves send abnormal signals that the brain interprets as pain.

**CURRENT TREATMENT:** No effective drug

**OPPORTUNITY:** Inhibiting the pain signals that induce abnormal pain could result in an effective therapeutic for the one million patients who experience these chronic pain symptoms every year.

## PERITUMORAL BRAIN EDEMA

**DESCRIPTION :** Brain swelling caused by a tumor, leading to neurological impairment such as seizures, muscle weakness, loss of coordination, and double vision.

**CURRENT TREATMENT:** Synthetic corticosteroids

**LIMITATIONS:** Serious side effects at the high, chronic doses needed to be effective: psychosis, muscle wasting, osteoporosis, and vision problems.

**OPPORTUNITY:** A safe, effective anti-swelling agent would enhance the quality of life of the estimated 100,000 patients diagnosed in the U.S. each year with brain tumors. The FDA recognized the medical need by granting XERECEPT<sup>™</sup> orphan drug designation for this condition.

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THE WALL STREET TRANSCRIPT  
100 Wall Street, New York, NY 10005

Tel: (212) 952-7400 • Fax: (212) 668-9842; (212) 668-9858; (212) 490-3258  
Website: <http://www.twst.com> • E-mail: [twst@worldnet.att.net](mailto:twst@worldnet.att.net)

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