

Emerging Company Profile

TauTaTis: Tau now

By **Michael Flanagan**
Senior Writer

Building on years of incremental progress in research on small molecule kinase inhibition for CNS disorders, **TauTaTis Inc.** was formed last year to develop a preclinical program designed to address the underlying pathologies of neurodegenerative conditions including Alzheimer's and Parkinson's diseases.

The company's TTT-3002 is a small molecule that inhibits a pair of undisclosed kinase families associated with the MAP kinase pathway. TauTaTis believes the compound blocks the aberrant hyperphosphorylation of tau, a process thought to play a key role in neuronal degeneration.

Tau stabilizes axonal microtubules that normally facilitate intracellular neuronal trafficking. In neurodegenerative diseases, tau becomes abnormally phosphorylated and loses its ability to maintain the structures of microtubules, eventually aggregating into filaments and neurofibrillary tangles (NFTs).

Hanno Roder, chairman and president of TauTaTis, has been studying abnormal phosphorylation in the brain since he was a post doc at **Massachusetts Institute of Technology** in the late 1980s, eventually focusing on tau and its relevance for neurodegeneration. He continued this work at **Bayer AG** and later at German startup Nadag AG, which was subsequently acquired by Sirenade Pharmaceuticals AG (now part of **KeyNeurotek AG**).

While at Bayer, Roder discovered an undisclosed "pathological aspect" of the MAP kinase pathway that he believed was related to neurological disorders, particularly Alzheimer's (AD). However, the pharma shelved its CNS work in the late 1990s and Nadag was acquired in 2004. Thus, Roder took his early stage work to the **Mayo Clinic's** Florida campus to work with Michael Hutton, who was developing transgenic mouse models of abnor-

TauTaTis Inc.

Jacksonville, Fla.

Technology: Small molecule kinase inhibitors to treat neurodegenerative diseases and cancer

Disease focus: Neurology, cancer

Clinical status: Preclinical

Founded: 2004 by Hanno Roder

University collaborators: University of Cincinnati

Corporate partners: None

Number of employees: 1

Funds raised: \$550,000

Investors: Private investors

President: Hanno Roder

Patents: 1 issued, covering the use of kinase inhibitors for Alzheimer's disease

mal tau brain pathology.

According to Roder, cell and tissue models of tau hyperphosphorylation support the company's hypothesis that TTT-3002 is capable of clearing mutant tau by blocking MAP kinase pathways. "We also verified that it has good brain penetration, is orally bioavailable and can be dosed as a solid, has a reasonable half-life, and can be dosed in mice for long periods of time with no toxicities," he said.

One surprise that emerged from *in vitro* work this year was that TTT-3002 also blocked leucine-rich repeat kinase 2 (LRRK2), a second protein family involved with the MAP kinase pathway. "We initially found that it inhibits homologs of LRRK2, suggesting it would also work against this protein, which it did," said Roder. "In fact, it turned out to be about as potent an inhibitor for LRRK2 as a kinase inhibitor can ever become."

As mutations in LRRK2 have been identified as the most common genetic

association with Parkinson's (PD), TauTaTis now hopes to expand its development plan beyond AD.

"We have a much deeper scientific understanding about the Alzheimer's story for TTT-3002 at this point, but for Parkinson's we have a very compelling target that is clear cut," Roder told BioCentury.

TauTaTis expects proof of principle results for AD in mice next spring. It will be a key inflection for the program, Roder said.

"Unlike in Parkinson's, where we can go back and modify the selectivity to focus on the LRRK2 effects, for Alzheimer's there is no back-up plan, he said. "Either TTT-3002 works" in AD, or the indication will be shelved.

Also next spring, the company expects data for TTT-3002 in a worm model of PD.

"If all goes to plan, 2011 is a reasonable expectation for Phase I testing to start" in healthy volunteers, said Roder.

TTT-3002 also has shown anti-proliferative activity in xenograft models of cancer.

"We haven't worked out the molecular mechanism in a way that could be published at this point, but the compound's potential in oncology is something that we'll continue to develop," though it will take a back seat to the neurodegenerative indications, Roder said.

TauTaTis has raised \$550,000 from private investors. Roder said he hopes to fund operations primarily through SBIR money and NIH grants.

COMPANIES AND INSTITUTIONS MENTIONED

Bayer AG (Xetra:BAY), Leverkusen, Germany

KeyNeurotek AG, Magdeburg, Germany

Massachusetts Institute of Technology, Cambridge, Mass.

Mayo Clinic, Jacksonville, Fla.

TauTaTis Inc., Jacksonville, Fla.

University of Cincinnati, Cincinnati, Ohio

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