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Emerging Company Profile

Zocere: Stepping up in stroke

By Lauren Martz
Staff Writer

Zocere Inc. may have found a new way to decrease ischemic brain injury in patients following stroke. The company is developing an injectable, degradation-resistant version of the neuroprotective STEP peptide that could improve patient outcomes when given up to six hours after the event, longer than the lone marketed stroke drug.

Protein tyrosine phosphatase non-receptor type 5 (PTPN5; STEP) is a downstream regulator of the NMDA receptor pathway. Activation of the NMDA receptor following stroke causes activation of p38 mitogen-activated protein kinase (p38 MAPK; MAPK14), excessive nitric oxide (NO) production and a neuronal excitotoxic response that contributes to cell death.

When STEP is activated by the NMDA receptor NR1 and NR2B subtypes, the peptide binds and blocks activation of p38 MAPK to dampen the neuronal excitotoxic response.

STEP is up-regulated following stroke, but Surojit Paul and colleagues found the peptide is quickly phosphorylated and degraded following ischemic injury, allowing the spread of neuronal damage. Paul is associate professor of neurology and neuroscience at the **University of New Mexico** and inventor of Zocere's technology.

Zocere Inc.

Albuquerque, N.M.
Technology: STEP-based peptide to treat ischemic stroke
Disease focus: Neurology
Clinical status: Preclinical
Founded: 2013 by New Mexico Angels Inc.
University collaborators: University of New Mexico
Corporate partners: None
Number of employees: 2
Funds raised: $250,000
Investors: New Mexico Angels and an undisclosed private equity fund
CEO: Wayne Laslie
Patents: None issued

Paul's team has designed a STEP-based peptide that resists ubiquitin-dependent proteasomal degradation, penetrates the blood-brain barrier and may have a sustained neuroprotective effect.

Last year, the team reported in *The Journal of Neuroscience* that intravenous injection of the STEP-derived peptide before, during or up to six hours after ischemic injury decreased brain damage compared with control in a rat model of stroke.

The only approved drug for ischemic stroke, Activase alteplase from **Roche**'s **Genentech Inc.** unit, is indicated for use within three hours of stroke in the U.S., and within 4.5 hours of symptom onset in the EU. Activase is a recombinant tissue plasminogen activator (tPA) that targets the stroke-causing blood clot. **Boehringer Ingelheim GmbH** markets the drug as Actilyse in the EU.

"Despite advances in understanding the pathophysiology of cerebral ischemia, successful treatment remains a major challenge in clinical medicine," Paul told BioCentury. "Reperfusion with recombinant tissue plasminogen activator remains the only pharmacologic therapy. The development of neuroprotection strategies that amplify the time window for thrombolytic treatment is therefore an important goal."

STEP-based peptides may protect neurons from damage during both ischemia and reperfusion, as well as increase the treatment window for thrombolytic therapeutic administration, he said.

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Zocere Inc.,
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At least eight companies have stroke therapeutics with specific neuroprotective activity in Phase II testing or earlier, including three that specifically target the NMDA pathway.

NoNO Inc.'s NA-1 is a peptide that inhibits discs large homolog 4 (DLG4; PSD95), which lies downstream of the NMDA receptor. It is in Phase II testing.

Xigen S.A.'s Phase I candidate XG-102 is an inhibitor of the c-jun N-terminal kinase (JNK), another downstream regulator of NMDA receptor signaling.

"It is most likely that PSD-95, the STEP-derived peptide and JNK will act at different stages of an ischemic insult," said Zocere CEO Wayne Laslie.

Global Neurotech (GNT) Pharma Co. Ltd.'s Neu2000 also is in Phase I. It is an NR2B-selective antagonist.

According to the literature, blocking the NMDA receptor directly would disrupt its other physiological functions, including normal neurotransmission, causing CNS side effects ranging from confusion to psychosis. However, selectively targeting the NR2B subunit of the receptor responsible for neuronal excitotoxicity may decrease the impact on other physiological functions.

Zocere is in the process of acquiring a patent application from the university covering the STEP-based peptide.

The next steps, according to Paul, are testing the peptide in models of long-term recovery and of stroke with significant comorbidities. The company is working on pharmacology, toxicology and GMP studies.

Laslie said the goal is to file an IND within three to five years. The company will initially focus on ischemic stroke.

Zocere has raised $250,000 from angel investors and an undisclosed private equity technology fund and has a commitment from the private equity group for an additional $200,000.

The company hopes to raise a further $1 million to finish pharmacology and toxicology studies this year, and an additional $1.5-$2 million per year in 2015 and 2016 to finish the GMP studies.

COMPANIES AND INSTITUTIONS MENTIONED

Boehringer Ingelheim GmbH, Ingelheim, Germany
Genentech Inc., South San Francisco, Calif.
Global Neurotech (GNT) Pharma Co. Ltd., Yongin-si, South Korea
NoNO Inc., Toronto, Ontario
Roche (SIX:ROG; OTCQX:RHHBY), Basel, Switzerland
Zocere Inc., Albuquerque, N.M.
University of New Mexico, Albuquerque, N.M.
Xigen S.A., Epalinges, Switzerland