

For Immediate Release
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ZZ Biotech Announces Phase 2 Trial with 3K3A-APC in Stroke; Funds Will Be Provided by NIH and Broadview Ventures

HOUSTON, April 22, 2014—ZZ Biotech today announced that the National Institutes of Health will support a multicenter Phase 2 clinical trial of its experimental drug, 3K3A-APC, in patients suffering from acute ischemic stroke.

The Phase 2 study will evaluate safety, tolerability and activity of ZZ Biotech's 3K3A-APC when given after tissue plasminogen activator, or tPA, in patients who have experienced moderately severe ischemic stroke. The drug will be given intravenously as a 15-minute infusion every 12 hours for up to five treatments, and four dose levels will be evaluated. About 100 participants, ages 18 to 80, will be followed for 90 days.

The experimental drug 3K3A-APC is a genetically engineered variant of the naturally occurring activated protein C, which plays a role in the regulation of blood clotting and inflammation. In animal models of stroke, 3K3A-APC has helped prevent bleeding caused by tPA the only drug currently indicated for the treatment of acute ischemic stroke.

Patrick Lyden, MD, chair of the Department of Neurology at Cedars-Sinai, will be the principal investigator of the NIH-supported study in stroke patients, which is expected to begin recruiting patients across the country in the second half of this year.

“There are few medical disorders that can have the sudden, potentially devastating consequences we often see with stroke,” said Lyden. “When treated quickly with the already-approved clot-busting drug tPA, the effects of many ischemic strokes can be reversed, but the time window of opportunity is short, and the treatment is not without risks. This study will help determine if the addition of 3K3A-APC can improve outcomes and reduce treatment side effects.”

ZZ Biotech scientific co-founder Berislav Zlokovic, MD, PhD, director of the Zilkha Neurogenetic Institute at the Keck School of Medicine of the University of Southern California, will be a study co-investigator.

“From the beginning, our intent has been to bring promising scientific discoveries from the laboratory bench to the patient bedside, where they have the most impact,” said Zlokovic, who continues to study 3K3A-APC's other potential applications at USC. “We are pleased to have this opportunity to continue our work in translational medicine and save more lives.”

The new drug originated in the laboratory of John Griffin, PhD, professor in the Department of Molecular and Experimental Medicine at The Scripps Research Institute, which licensed development rights to ZZ Biotech.

In conjunction with this announcement, ZZ Biotech also announced that it has received its first venture capital investment from Broadview Ventures, a Boston-based philanthropic venture firm focused on investments in cardiovascular disease and stroke. ZZ Biotech was founded in 2006 by Zlokovic and financier and philanthropist Selim Zilkha, and has been funded to date by private investors and a Qualifying Therapeutic Discovery Project grant.

Joseph Romano, ZZ Biotech CEO, said: “We have been fortunate to have a wonderful group of investors dedicated to seeing us through the development of this important new potential drug for stroke, and we are pleased to welcome Broadview Ventures into our investor group. Funds provided by Broadview Ventures and NIH will allow us to conduct our first clinical study in actual stroke patients. We are gratified that both of these groups, each with discerning subject-matter experts in neurovascular disease treatments, recognize the potential of our drug to have a profound impact on the treatment of stroke.”

“Broadview Ventures’ mission is to accelerate the development of promising technology to effect meaningful change for patients. We are very pleased to add ZZ Biotech to our growing neurovascular portfolio,” stated Chris Colecchi, Managing Director at Broadview Ventures. “We are especially pleased that this promising science is being supported so strongly by the NIH.”

The NIH National Institute of Neurological Disorders and Stroke (NINDS) has awarded a clinical trial grant to Cedars-Sinai and a NeuroNEXT Infrastructure Resource Access award to ZZ Biotech. Kent Pryor, PhD, the company’s chief operating officer, will be the principal investigator for the NeuroNEXT aspect of the study, which permits ZZ Biotech to contribute financial and operational support and enlist the collaboration of this NINDS-funded research network.

“We are very pleased that NINDS selected our study to be conducted within NeuroNEXT,” said Pryor. “We are looking forward to continuing our productive collaboration with Dr. Lyden and working with the NeuroNEXT team to answer critical questions about the effects of 3K3A-APC in patients suffering from acute ischemic stroke.”

NINDS created [NeuroNEXT](#) – the Network for Excellence in Neuroscience Clinical Trials – to increase its ability to explore promising treatments by partnering with academia, private foundations and industry. With the support of the announced grant awards, the researchers will have access to the NeuroNEXT Clinical Coordinating Center at Massachusetts General Hospital and the Data Coordinating Center at the University of Iowa. The University of Rochester in New York will provide a central laboratory, and about 15 NeuroNEXT centers nationwide will participate in the study.

About ZZ Biotech

ZZ Biotech is a company headquartered in Houston, Texas, with a mission to develop innovative biological treatments for the aging and damaged brain, including those affected by stroke and other neurodegenerative disorders. ZZ Biotech is developing a genetically engineered variant of recombinant human activated protein C (APC), named 3K3A-APC, that has reduced anticoagulant activity, but preserved cell-protective and anti-inflammatory activities compared to wild-type APC. ZZ Biotech's first Phase 1 clinical trial of 3K3A-APC is complete and the company expects to commence a Phase 2 clinical trial in stroke patients in 2014 in partnership with NeuroNEXT.

About Broadview Ventures

In 2008 the Leducq Family Trust established Broadview Ventures, Inc. with the mission to accelerate the development of promising technology in cardiovascular and neurovascular disease through targeted investments in and support of early stage ventures. By making funding available at a critical moment in the development of new technology, the Leducq Family Trust is taking a leadership position in venture philanthropy by finding creative ways to support translational research in order to bring the advancements of science to the care of patients.

About 3K3A-APC

ZZ Biotech's 3K3A-APC is a genetically engineered variant of the naturally occurring activated protein C, which plays a role in the regulation of blood clotting and inflammation. APC has cell-protecting, anti-inflammatory and anti-coagulant properties; 3K3A-APC has reduced anti-coagulant ability, which minimizes the risk of bleeding induced by unmodified APC. In animal models of stroke, amyotrophic lateral sclerosis (ALS), neurotrauma, and sepsis, 3K3A-APC therapy has shown an advantage over recombinant APC in enhanced efficacy and reduced risk for bleeding. The protective effect of 3K3A-APC on the lining of blood vessels in the brain further helps prevent bleeding sometimes caused by tissue plasminogen activator, or tPA, the only drug currently indicated for the treatment of acute ischemic stroke.

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Literature Reference for the Phase 1 Study

Lyden P, Levy H, Weymer S, Pryor K, Kramer W, Griffin JH, Davis TP, Zlokovic B (2013) Phase 1 Safety, Tolerability and Pharmacokinetics of 3K3A-APC in Healthy Adult Volunteers. *Curr Pharm Des.* 19 (42), 7479-7485. PMID: [24372304](https://pubmed.ncbi.nlm.nih.gov/24372304/)

Phase 2 Study Title

ZZ-3K3A-201: A multi-center, Phase 2 study using a continual reassessment method to determine the safety and tolerability of 3K3A-APC, a recombinant variant of human



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activated protein C (APC), in combination with tissue plasminogen activator (tPA) in moderately severe acute hemispheric ischemic stroke