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ZZ Biotech Announces FDA Fast Track Designation for Stroke Program

HOUSTON, June 12, 2020—ZZ Biotech today announced that the US Food and Drug Administration (FDA) has designated the investigation of the company's experimental drug 3K3A-APC for the treatment of acute ischemic stroke as a Fast Track development program.

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. 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. The NIH National Institute of Neurological Disorders and Stroke (NINDS) sponsored a Phase 2 clinical trial in acute ischemic stroke patients called RHAPSODY through a clinical trial grant to Cedars-Sinai (Dr. Patrick Lyden, Principal Investigator) and a NeuroNEXT Infrastructure Resource Access award to ZZ Biotech. The results of the study were published in *Annals of Neurology* in 2019. All doses were deemed safe and well-tolerated, and total hemorrhage volume and hemorrhage incidence were both substantially reduced in 3K3A-APC treated patients.

FDA Fast Track is a process designed to facilitate the development and expedite the review of drugs to treat serious conditions and fill an unmet medical need. The purpose is to get important new drugs to the patient earlier. Fast Track addresses a broad range of serious conditions.

A drug that receives *Fast Track* designation is eligible for some or all of the following:

- More frequent meetings with FDA to discuss the drug's development plan and ensure collection of appropriate data needed to support drug approval;
- More frequent written communication from FDA about such things as the design of the proposed clinical trials and use of biomarkers;
- Eligibility for *Accelerated Approval and Priority Review, if relevant criteria are met;* and
- *Rolling Review*, which means that a drug company can submit completed sections of its Biologic License Application (BLA) or New Drug Application (NDA) for review by FDA, rather than waiting until every section of the NDA is completed before the entire application can be reviewed. BLA or NDA review usually does not begin until the drug company has submitted the entire application to the FDA.

"We are very pleased the FDA has recognized the potential of 3K3A-APC to address unmet medical needs in the treatment of acute ischemic stroke," said Dr. Kent Pryor, CEO of ZZ Biotech. "Stroke is a serious condition that extracts a heavy toll on patients and their families, as well the greater healthcare system. We look forward to working collaboratively with FDA to continue the development of 3K3A-APC in the treatment of acute ischemic

stroke in a Phase 3 clinical study and bring a new treatment to patients as rapidly as possible."

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.

NIH-funded preclinical development of the drug for stroke and other neurological indications was carried out in the laboratory of Berislav Zlokovic, MD, PhD, director of the Zilkha Neurogenetic Institute and professor and chair of the Department of Physiology and Neuroscience at Keck School of Medicine of the University of Southern California. Zlokovic, who was scientific founder of ZZ Biotech, was also a co-investigator on the Phase 2 study.

About ZZ Biotech
ZZ Biotech, LLC is a clinical stage company developing innovative biologic treatments for ischemic stroke and other neurological diseases and wound healing applications including the treatment of diabetic foot ulcers. Headquartered in Houston, 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 has completed a Phase 2 study in acute ischemic stroke 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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Phase 2 Publication Reference
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2 Trial Using a Continual Reassessment Method to Determine the Safety and Tolerability of 3K3A-APC, A Recombinant Variant Human Activated Protein C, in Combination with Tissue Plasminogen Activator, Mechanical Thrombectomy or both in Moderate to Severe Acute Ischemic Stroke. *Annals of Neurology*. 2019; *85:*125-136.
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