CytoDel Announces Pre-Clinical Data on Cyto-111 as Antidote to Botulinum Neurotoxin (BoNT) Published in *Science Translational Medicine*

Studies Show Cyto-111 Enables Delivery of Antibodies to Previously Inaccessible Intraneuronal Targets without the need for a Viral Vector or Transfection

Supports the Development of New Approaches to Treat Multiple Neurological Diseases

New York City, January 6, 2021 – CytoDel, Inc. ("CytoDel" or "the Company"), a privately-held corporation, today announces the publication of preclinical data on the Company's lead product, Cyto-111, in the peer-reviewed journal, *Science Translational Medicine*. The complete text of the article titled, "Neuronal Delivery of Antibodies has Therapeutic Effects in Animal Models of Botulism," can be found here.

Cyto-111 was conceived, expressed and purified in the laboratory of Konstantin Ichtchenko, Ph.D., NYU Grossman School of Medicine, Department of Biochemistry and Molecular Pharmacology, who was a principal investigator in the study, which was supported by grants from the National Institute of Allergy and Infectious Diseases (NIAID), a division of the National Institute of Health (NIH).

Based on Dr. Ichtchenko's hypothesis that the C1*ad* delivery vehicle previously reported could be used to transport therapeutic proteins into the neuronal cytosol, researchers led by Dr. Ichtchenko developed and tested a potential treatment for botulism based on intracellular inhibition of the BoNT subtype A1 light chain metalloprotease (LC/A1). The main objective of the study was to develop and test a post-symptomatic botulism antidote that could rescue symptomatic animals challenged with a lethal dose of BoNT. Following *in vitro* validation of therapeutic mechanisms, efficacy studies were conducted in mice, guinea pigs and rhesus macaque monkeys.

The study showed that a precision biotherapeutic consisting of a function-blocking single domain antibody (sdAb; B8) cargo fused to the C1*ad* delivery vehicle (forming B8C1*ad* or Cyto-111) can enter neurons and protect SNARE proteins by inhibiting LC/A1 catalytic activity in situ. Post-symptomatic administration of B8C1*ad* produced antidotal rescue in mice, guinea pigs, and non-human primates following a lethal botulism challenge.

According to the study's authors, "The flexibility of the C1*ad* molecular delivery platform offers several advantages for the rapid generation of new treatments for neurological disorders. In particular, the presynaptic localization of LC suggests this therapeutic approach will be particularly effective in treating synaptopathies involving active zone proteins. Indeed, the platform can be efficiently redirected towards other protein targets by replacing or adding single domain antibodies or other protein moieties."

The study concluded that, "These data demonstrate that atoxic BoNT derivatives can be harnessed to deliver therapeutic protein moieties to the neuronal cytoplasm where they bind and neutralize intracellular targets in experimental models. The generalizability of this platform might enable delivery of antibodies and other protein-based therapeutics to previously inaccessible intraneuronal targets."

"This is a landmark study in converting the power of lethal botulinum neurotoxins into therapies. The approach used to turn botulinum toxin into a kind of Trojan horse that delivers a cargo into neurons has enormous potential for future drug development," noted Thomas C. Südhof, M.D., Professor in the School

of Medicine in the Department of Molecular and Cellular Physiology, and in Neurology, Psychiatry and Behavioral Sciences at Stanford University, a 2013 Nobel Prize winner in Physiology/ Medicine, a Howard Hughes Medical Institute investigator, and Chair of CytoDel's Scientific Advisory Board.

"We are delighted to have these data published in a well-respected peer-reviewed journal as they represent the culmination of many years of research with the intent of finding a solution to effectively treat weaponized botulinum toxins. Importantly, these groundbreaking data are the result of the efforts of researchers from a number of renowned institutions including NYU Grossman School of Medicine, Cummings School of Veterinary Medicine at Tufts University, and the US Army Medical Research Institute for Chemical Defense, without whose hard work and dedication this achievement would not have been possible," commented Phillip A. Band, Ph.D., Research Professor in the Departments of Orthopedic Surgery, Biochemistry and Molecular Pharmacology, NYU Grossman School of Medicine, and co-inventor, co-founder and Chief Executive Officer of CytoDel.

"Not only did these studies show that Cyto-111 can be an antidote to botulinum toxins, but they demonstrate the generalizability of the molecular vehicle in three different species to safely and effectively deliver functional antibodies to the inside of neurons via a non-viral mechanism. This is a particularly exciting breakthrough as no other labs have previously inactivated a pathogen inside of neurons, which are inaccessible to standard antibodies. This achievement opens the door for the development of new approaches to treat multiple neurological diseases," added Dr. Band.

About Botulinum Neurotoxin

Botulinum neurotoxin (BoNT) is considered a Tier 1 weapon of mass destruction. BoNT has no odor or taste, a single gram is sufficient to kill 1 million humans via ingestion or inhalation, and currently there are no treatments to reverse symptoms. All currently available treatments for botulism are antibody products which can only neutralize toxin in the systemic circulation. Once the toxin has entered the neurons controlling respiration, generally 24-72 hours after exposure depending on the dose, antibody-based products become ineffective. Standard antibodies cannot access toxin already inside neurons, and thus BAT® (Botulism AntiToxin, a product of Emergent BioSolutions), the only FDA-approved antitoxin, is only effective while the toxin remains in the circulation.

About Cyto-111

Cyto-111 uses CytoDel's Intraneuronal Delivery Platform to deliver an antibody to the inside of BoNT-intoxicated neurons, thereby allowing rescue after the toxin has entered neurons and is causing symptoms. This "Trojan horse" approach uses an inactivated recombinant BoNT derivative to carry the antibody to the inside of BoNT-intoxicated neurons. Cyto-111 can uniquely reverse symptoms because it can deliver its antibody to toxin already inside the neuron. In biodefense scenarios, this significantly extends the period post-exposure during which treatment can reverse symptoms and can save lives by minimizing the need for long-term artificial respiration. As a therapeutic for naturally occurring botulism, Cyto-111 extends the therapeutic window beyond the current 48-hour limit during which BAT has proven to be effective.

About CytoDel

CytoDel is a privately held biopharmaceutical company that uses the tools of 21st century molecular biology to produce recombinant derivatives of botulinum neurotoxin customized to specific applications. The Company's proprietary technology allows CytoDel to manipulate the BoNT molecule to develop next generation BoNT products and a drug delivery vehicle that can deliver therapeutic molecules to the inside of neurons. CytoDel's lead program is focused on developing BioBetter BoNT pharmaceuticals, offering improved safety margin and effectiveness outcomes for the treatment of large muscles and muscle

groups. A second program utilizes intraneuronal delivery for Biodefense, and CytoDel is also developing programs for the treatment of nervous system disorders and chronic pain. For more information visit www.cytodel.com.

* Both Drs. Ichtchenko and Band from NYU Grossman School of Medicine have financial interests in CytoDel and Dr. Band serves on its management team. These arrangements are being managed in accordance with the policies and practices of NYU Langone Health.

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