



1<sup>st</sup> of February, 2022

Axcelead, Inc.

Tokyo Medical and Dental University

## **Axcelead Begins Joint Research with Tokyo Medical and Dental University on mRNA Drug Development for Acute Cerebral Infarction and Postresuscitation Encephalopathy**

Axcelead, Inc. (President & CEO: Tomoyuki Fujisawa, “Axcelead”) has signed a joint research agreement with Tokyo Medical and Dental University (President: Yuichiro Tanaka, “TMDU”) in order to develop a mRNA therapeutics encoding brain-derived neurotrophic factor (“BDNF”) for the curative treatment of ischemic central nervous system disease, such as acute cerebral infarction and postresuscitation encephalopathy. Axcelead and TMDU will conduct none-clinical studies using animal models and aim to obtain clinical development candidate molecules for BDNF mRNA therapeutics. BDNF mRNA is expected to enable the world's first curative therapy for ischemic central nervous system diseases with extremely high medical needs.

### **【Background】**

Stroke is the second leading cause of death with approximately 5.5 million deaths in 13 million cases annually in worldwide, and with about 60,000 deaths in more than 1 million cases in Japan. Ischemic central nervous system disease accounts for majority of stroke patients. Despite its extremely high medical needs, there is no proven effective treatment that can prevent neuronal death after the ischemia. This joint research is on mRNA drug development targeting ischemic central nervous system disease, which causes neurological dysfunction due to nerve cell death induced by decreased blood flow. The current treatment for this disease is limited to symptomatic one that suppresses the some of the cause of nerve cells. There is no neuroprotective or neuronal proliferative therapeutics for clinical applications.

In this joint research, we are aiming to obtain clinical development candidate molecules for BDNF mRNA therapeutics. BDNF is an endogenous humoral protein found in wide range of organism. Human BDNF was identified more than 30 years ago. From various research results including clinical studies, it has been elucidated that BDNF is a member of the neurotrophin family of growth factors, that enhance neuronal survival and function. On the other hand, despite several attempted clinical trials with BDNF as recombinant protein formulation, there is no successful result due to the extremely low blood stability and the



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technical difficulty in delivering the BDNF protein into the brain.

Messenger RNA therapeutics, a most recent clinically proven and promising modality, can express the functional target protein by delivering mRNA to the target organ. Based on the previous research activities by Professor Itaka and others, the delivery of BDNF mRNA into the brain and improvement of neurological dysfunction due to ischemic injury by local expression of the BDNF protein by using animal model have been confirmed <sup>(1)</sup>. In this joint research, we aim to obtain mRNA therapeutics candidates by further developing the TMDU's previous research activities, optimizing BDNF mRNA sequence, and optimizing carriers that deliver BDNF mRNA into the brain.

#### 【Role of Axcelead】

ARCALIS, (<https://corp.arcalis.co.jp/en>) which is the subsidiary of Axcelead, operates only one-stop mRNA contract development and manufacturing (CDMO) business in Japan and now they are working on the establishment of mRNA API and drug product manufacturing plants, respectively\*. ARCALIS has in-licensed mRNA manufacturing technology from Arcturus in May 2021, and expects to have operational manufacturing capability beginning in 2022.

This project will utilize the intellectual property, human resources, and facilities of ARCALIS and Axcelead DDP, which is also a group company of Axcelead, to develop safe and highly effective mRNA formulations suitable for pharmaceutical use by examining mRNA sequences and carriers provided by Axcelead, in addition to the mRNA drug delivery technology that has been studied by Professor Keiji Itaka and his colleagues at TMDU.

#### 【Researcher profile】

Keiji Itaka, M.D., Ph.D., Professor, Department of Biofunction Research, Institute of Biomaterials and Bioengineering, Tokyo Medical and Dental University(TMDU) Area of study - DDS (Drug Delivery System) , gene therapy, nucleic acid medicine, biomaterials

#### 【About Axcelead】

Axcelead, Inc. is a group of companies that develops a drug discovery platform business;

- Axcelead Drug Discovery Partners, Inc. (ADDP) (<https://www.axcelead.com/en/>) – Japan's first integrated drug discovery solution provider, which took over Takeda's drug discovery platform business in 2017
- ARCALIS (<https://corp.arcalis.co.jp/en>) which operates Japan's only one-stop mRNA contract development and manufacturing (CDMO) business,



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- PassPort Technologies (<https://passport-tech.com/>) ,which has next-generation transdermal drug delivery technology.

Axcelead, is the flagship portfolio company of Drug Discovery Gateway Fund, which was jointly established by Whiz Partners, Inc., and Takeda Pharmaceutical Company, Co., Ltd., in 2018, with the aim of promoting the drug discovery ecosystem in Japan and will make various contributions to healthcare broadly and globally. For more information on Axcelead, please visit the company's website at <https://www.axcelead-hd.com/>

[Reference]

( 1 ) Fukushima Y, Uchida S, Imai H, Nakatomi H, Kataoka K, Saito N, Itaka K.  
Treatment of ischemic neuronal death by introducing brain-derived neurotrophic factor mRNA using polyplex nanomicelle. Biomaterials 270: 120681, 2021