PRESS RELEASE

For immediate release

NUS Medicine researchers develop potential oral anti-diabetic drug

- **DAA-1 improves action of insulin and reduces damaging chronic inflammation that accompanies diabetes**

- **Drug is developed by Department of Pharmacology, NUS Yong Loo Lin School of Medicine**

Singapore, 20 October 2016 – After 20 years of extensive research, a made-in-Singapore oral anti-diabetic drug has been developed by the Department of Pharmacology of the NUS Yong Loo Lin School of Medicine (NUS Medicine). Working together with the Singapore Clinical Research Institute (SCRI) and the National University Health System (NUHS), the team behind DAA-1's development today announced the successful completion of a Phase I clinical trial of the anti-diabetic drug.

How DAA-1 works

In normal individuals, insulin that is released from the pancreas after a meal binds to insulin-sensitive cells and activates the insulin pathway. This insulin pathway is connected to a glucose transporter, and when activated by insulin the pathway brings the glucose transporter from the inside of the cell to its surface. At the surface, the glucose transporter is then able to transport glucose from the blood into the cell for energy usage or storage. In diabetes, this pathway is

faulty and becomes resistant to insulin (i.e. the cell develops insulin resistance or does not response to insulin). There are switches in the insulin pathway connecting insulin to the glucose transporter that malfunction in diabetes. The result is that insulin loses its ability to initiate uptake of glucose into the cell. DAA-I rectifies all the four switches found to be malfunctioning in diabetes, said Associate Professor Sim Meng Kwoon, retired faculty member of the Department of Pharmacology at NUS Medicine and one of the lead investigators who carried out the study.

"Chronic inflammation in diabetes damages the endothelial lining of blood vessels, leading to vascular and organ damage - e.g. cardiovascular diseases, damage of retina leading to blindness, damage of the nephrons leading to kidney failure, damage of nerves leading to neuropathy. Thus, the importance of reducing chronic inflammation in diabetic individual is critical," he added.

"The drug molecule, des-aspartate-angiotensin I (DAA-I), is an endogenous angiotensin peptide, which acts on the angiotensin AT_1 receptor and produces biological responses that improve the action of insulin (i.e. attenuation of insulin resistance) leading to increased uptake of glucose into insulin-sensitive cells. Concurrently, DAA-I also reduces the damaging chronic inflammation that accompanies diabetes and attenuates pancreatic beta cell death."

Clinical studies

The single-dose Phase I trial, involved 18 healthy individuals, aged 24 years old to 47 years old, and was carried out from end September to December 2015 at the NUHS Investigational Medicine Unit together with SCRI, which provided project management and supported trial monitoring. The trial was led by Clinical Principal Investigator, Professor Lee Kok Onn from NUS Medicine's Division of Endocrinology.

Said Prof Lee, who is also a Senior Consultant at the National University Hospital's Division of Endocrinology, "The current anti-diabetic drugs target mainly the lowering of the blood glucose in diabetes, and generally lack the specificity of improving the action of insulin and reducing chronic inflammation in peripheral tissues."

The clinical trial successfully established that DAA-I was well tolerated by human subjects and this paves the way for further clinical trials on DAA-I, which the SCRI will continue to partner the NUHS and NUS Medicine.

“We are privileged to collaborate with both A/Prof Sim and Prof Lee on this landmark clinical trial which showcases the capabilities of Singapore in the drug development field. This study demonstrated the strong partnership between Singaporean research organisations in developing new drugs to treat common chronic diseases like diabetes mellitus, which affects about 11% of our adult population aged 18 to 69[1]”, said Associate Professor Teoh Yee Leong, a Public Health Physician and also SCRI’s Chief Executive Officer.

Further studies

The DAA-1 team aims to recruit 18 normal healthy subjects and 6 to 8 diabetic patients for a 14-day multi-dose Phase 1 trial in their next stage of the study. This will be followed by a Phase 2A trial involving 24 to 28 diabetic patients for a period of 3 months.

"This is a good example of how fundamental drug discovery and development research bridges the translational gap from basic pharmacological science to clinical trials,” said Professor Fred Wong, Head of the department of Pharmacology, NUS Medicine.

Diabetes Mellitus is one of the most prevalent chronic diseases in Singapore, with one in nine Singaporeans suffering from diabetes[2]. The number of diabetic people in Singapore is expected to grow from 400,000 in 2013 to 600,000 by 2030[3]. The global prevalence of diabetes is also estimated to be 9% among adults[4].

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[1] https://www.moh.gov.sg/content/moh_web/home/statistics/Health_Facts_Singapore/Disease_Burden.html

[2] http://www.diabetes.org.sg/

[3] http://www.healthxchange.com.sg/healthyliving/ManagingChronicIllnesses/Pages/diabetes-singapore-stats-prevention-tips.aspx

[4] http://www.who.int/mediacentre/factsheets/fs312/en/

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About National University of Singapore (NUS)

A leading global university centred in Asia, the National University of Singapore (NUS) is Singapore's flagship university, which offers a global approach to education and research, with a focus on Asian perspectives and expertise.

NUS has 17 faculties and schools across three campuses. Its transformative education includes a broad-based curriculum underscored by multi-disciplinary courses and cross-faculty enrichment. Over 38,000 students from 100 countries enrich the community with their diverse social and cultural perspectives.

NUS has three Research Centres of Excellence (RCE) and 29 university-level research institutes and centres. It is also a partner in Singapore's fifth RCE. NUS shares a close affiliation with 16 national-level research institutes and centres. Research activities are strategic and robust, and NUS is well-known for its research strengths in engineering, life sciences and biomedicine, social sciences and natural sciences. It also strives to create a supportive and innovative environment to promote creative enterprise within its community.

For more information on NUS, please visit www.nus.edu.sg.

About NUS Yong Loo Lin School of Medicine

Established in 1905, the NUS Yong Loo Lin School of Medicine is the first institution of higher learning in Singapore and the genesis of the National University of Singapore. The School offers one of the finest undergraduate medical programmes in the Asia Pacific region, led and taught by internationally respected faculty. The latest university rankings from Quacqarelli Symonds (QS) rate NUS Medicine as one of Asia's best. Globally, it is now ranked 21.

The School admits 300 students to its medical undergraduate degree programme annually while 100 students are enrolled in the nursing undergraduate degree programme. Research programmes at the School seek

to provide meaningful solutions to Singapore's healthcare needs. The 18 NUS Medicine departments in the basic sciences and clinical specialties work closely with the Alice Lee Centre for Nursing Studies and the Centre for Biomedical Ethics to ensure that teaching and research are aligned and relevant to Singapore's healthcare needs.

The School is part of the National University Health System.

For more information about the Yong Loo Lin School of Medicine, please visit http://medicine.nus.edu.sg

About Singapore Clinical Research Institute (SCRI)

Singapore Clinical Research Institute (SCRI) is a National Academic Research Organisation dedicated to enhance the standards of human clinical research. Its mission is to spearhead and develop core capabilities, infrastructure and scientific leadership for clinical research in Singapore. SCRI is a national clinical trials coordination centre that works with National Medical Research Council (NMRC) to assist the Ministry of Health in implementing clinical trials policy and strategic initiatives to support and develop clinical research competencies locally.

In driving towards its vision, SCRI collaborates with clinicians to enhance Singapore's clinical research and strengthen its expertise in executing multi-site, multi-national studies and the development of regional clinical research networks.

SCRI is a wholly-owned subsidiary of MOH Holdings. http://www.scri.edu.sg