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INSILICO MEDICINE

InSilico Medicine Cayman TopCo
英矽智能

(Incorporated in the Cayman Islands with limited liability)

(Stock code: 3696)

VOLUNTARY ANNOUNCEMENT ON COMPLETION OF FIRST PATIENT FIRST DOSE IN BETHESDA: A PHASE IIA TRIAL FOR GARUTADUSTAT (ISM5411)

This is a voluntary announcement made by InSilico Medicine Cayman TopCo (the "**Company**", together with its subsidiaries, the "**Group**").

The Company hereby informs the shareholders and potential investors of the Company of the attached press release that the Company has completed the first patient first dose in BETHESDA: a Phase IIa clinical trial of ISM5411, which has recently been granted the generic name of Garutadustat by the United States Adopted Names Council (USAN Council). Garutadustat (originally ISM5411) is a novel, gut-restricted PHD inhibitor developed with Pharma.AI, the Group's generative platform, for the treatment of Inflammatory Bowel Disease (IBD). BETHESDA, named Barrier Enhancement Therapy for Healing Enteric Structural Defects & Anomalies, an ongoing multicenter, randomized, double-blind, placebo-controlled Phase IIa trial of Garutadustat is led by Professor Minhu Chen (as Leading PI), one of the most renowned Gastroenterology experts in China and the subject leader of Department of Gastroenterology at the First Affiliated Hospital of Sun Yat-sen University. In approximately 80 participants with ulcerative colitis, BETHESDA plans to assess the safety, tolerability, and pharmacokinetics (PK) of Garutadustat, and efficacy signals will be monitored through clinical remission/response, endoscopy, histopathology, and biomarker exploration.

By order of the Board
InSilico Medicine Cayman TopCo
Mr. Aleksandrs Zavoronkovs, Ph.D.
Chairman, Executive Director and CEO

Hong Kong, January 12, 2026

As at the date of this announcement, the board of directors of the Company comprises Mr. Aleksandrs Zavoronkovs, Ph.D. and Mr. Feng Ren, Ph.D. as executive directors; Mr. Kan Chen, Ph.D., Mr. Chuen Yan Leung, Ph.D., and Mr. Long Shi as non-executive directors; and Mr. Jingsong Wang, Ph.D., Ms. Denitsa Milanova, Ph.D. and Mr. Roman Kyrychynskyi as independent non-executive directors.

Insilico Medicine Completes First Patient First Dose in BETHESDA: A Phase IIa Trial for Garutadustat (ISM5411), the Gut-restricted AI-driven PHD Inhibitor for the Treatment of Inflammatory Bowel Disease

Insilico Medicine ("**Insilico**"), a clinical-stage, generative AI-driven drug discovery company, today announced the completion of first patient first dose in BETHESDA: a Phase IIa clinical trial of ISM5411 (NCT07265570), which has recently been granted the generic name of Garutadustat by the United States Adopted Names (USAN) Council. Garutadustat (originally ISM5411) is a novel, gut-restricted PHD inhibitor developed with Pharma.AI, Insilico's generative platform, for the treatment of Inflammatory Bowel Disease (IBD).

Named Barrier Enhancement Therapy for Healing Enteric Structural Defects & Anomalies (BETHESDA), this ongoing multicenter, randomized, double-blind, placebo-controlled Phase IIa trial of Garutadustat is led by Professor Minhu Chen, one of the most renowned Gastroenterology experts in China and the subject leader of Department of Gastroenterology at the First Affiliated Hospital of Sun Yat-sen University. In approximately 80 participants with ulcerative colitis, BETHESDA plans to assess the safety, tolerability, and pharmacokinetics (PK) of Garutadustat, and efficacy signals will be monitored through clinical remission/response, endoscopy, histopathology, and biomarker exploration.

"Given the encouraging results from our Phase I studies on Garutadustat's safety and gut-restricted profile, we look forward to seeing how these benefits will be translated into ulcerative colitis patient population," says Carol Satler, MD, PhD, Senior Vice President for Clinical Development, Non-Oncology, Insilico Medicine. "This program is the output of an AI-driven breakthrough that sets a new benchmark in the field. We are excited to advance Garutadustat into Phase II trial and anticipate that its innovative, AI-identified mechanism will offer new hope for patients living with inflammatory bowel disease."

Inflammatory Bowel Disease (IBD) encompasses chronic, relapsing inflammatory conditions of the gastrointestinal tract, most notably ulcerative colitis and Crohn's disease. These diseases affect millions of people worldwide and can increase the risk of developing colitis-associated cancer, substantially impacting quality of life. However, existing therapies primarily focus on immune response modulation to relieve symptoms, and more than half of patients experience inadequate response or lose efficacy over time, sometimes facing an increased risk of infections. There remains a critical unmet need for novel therapies that not only alleviate inflammation but also foster long-term disease control and improved outcomes.

In January 2022, Garutadustat, the innovative, potentially best-in-class, oral PHD inhibitor was nominated as a preclinical candidate, within just 12 months, following the synthesis and screening of approximately 115 compounds through advanced AI-powered workflows assisted with Chemistry42, Insilico's proprietary generative chemistry engine.

With a novel structure empowered by AI, Garutadustat delivers a distinctive dual mechanism of action combining anti-inflammatory activity and enhanced repair of the intestinal barrier. Two completed Phase I studies in Australia and China indicate Garutadustat with favorable safety, tolerability, and gut-restrictive pharmacokinetic characteristics across all tested dose groups. In December 2024, the preclinical development of ISM5411 was published in Nature Biotechnology, underlining the innovation and translational potential of Insilico's AI-driven drug discovery platform.

Notably, Insilico Medicine recently licensed out ISM4808, a novel drug candidate also under the PHD program, to TaiGen Biotechnology for the treatment of anemia associated with chronic kidney disease (CKD). The out-licensing deal, with a total size of double-digit million dollars, leverages TaiGen's clinical and market expertise along with Insilico's AI-driven drug development efficiency and precision, aiming to satisfy the unmet medical needs.

By integrating the technologies of AI and automation, Insilico has demonstrated significant efficiency boost compared to traditional drug discovery methods (often requiring an average of 4.5 years), as announced in the recent key timeline benchmarks for internal programs from 2021 to 2024: the average time to PCC is 12-18 months, with 60-200 molecules synthesized and tested per program.

About Insilico Medicine

Insilico Medicine is a pioneering global biotechnology company dedicated to integrating artificial intelligence and automation technologies to accelerate drug discovery, drive innovation in the life sciences, and extend healthy longevity to people on the planet. The company was listed on the Main Board of the Hong Kong Stock Exchange on December 30, 2025, under the stock code 03696.HK.

By integrating AI and automation technologies and deep in-house drug discovery capabilities, Insilico is delivering innovative drug solutions for unmet needs including fibrosis, oncology, immunology, pain, and obesity and metabolic disorders. Additionally, Insilico extends the reach of Pharma.AI across diverse industries, such as advanced materials, agriculture, nutritional products and veterinary medicine. For more information, please visit www.insilico.com.