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HighTide Therapeutics, Inc.

君圣泰医药

(Incorporated in the Cayman Islands with limited liability)

(Stock Code: 2511)

HTD1801, A FIRST-IN-CLASS ANTI-INFLAMMATORY METABOLIC MODULATOR, DEMONSTRATES DURABLE 52-WEEK EFFICACY AND SAFETY IN COMPLETION OF TWO PHASE III TRIALS IN TYPE 2 DIABETES MELLITUS

This announcement is made by HighTide Therapeutics, Inc. (the “**Company**”, together with its subsidiaries, the “**Group**”) on a voluntary basis to inform the shareholders and potential investors of the Company about the latest business development of the Group.

The board of directors (the “**Board**”) of the Company announces positive 52-week efficacy and safety results from the open-label extension (OLE) phases of two Phase III trials (SYMPHONY-1 and SYMPHONY-2) evaluating HTD1801 in patients with type 2 diabetes mellitus (T2DM).

These 52-week data reinforce HTD1801’s potential as a truly differentiated therapeutic to concurrently address metabolic dysregulation, inflammation, and renal progression in type 2 diabetes mellitus

The 52-week data from these two Phase III clinical trials demonstrate the durability of response and highlight the comprehensive long-term clinical benefits of HTD1801 in patients with T2DM. HighTide plans to submit a new drug application (NDA) for HTD1801 as a treatment for T2DM to the Center for Drug Evaluation (CDE) of China’s National Medical Products Administration (NMPA) later this year.

SYMPHONY-1 (NCT06350890) and SYMPHONY-2 (NCT06353347) are randomized, double-blind, placebo-controlled, Phase III clinical trials designed to evaluate the efficacy and safety of HTD1801 in adults with T2DM and inadequate glycemic control despite diet and exercise (SYMPHONY-1; N=408) or with Metformin (SYMPHONY-2; N=551). The primary endpoint in both studies was the change in glycated hemoglobin (HbA1c) from baseline with HTD1801 compared to placebo after 24 weeks of treatment. Patients were eligible to continue in a 28-week OLE during which all patients received HTD1801; Durability of response across efficacy endpoints was evaluated based on the change from baseline to Week 52.

Efficacy observed during the 24-week double-blind period was durable and maintained with longer-term treatment through 52 weeks in both studies

SYMPHONY-1 (HTD1801 as monotherapy): At week 24, the reduction from baseline in HbA1c with HTD1801 (-1.3%) was superior to placebo. HbA1c reductions were maintained in patients who continued receiving HTD1801 (-1.2% at Week 52). Placebo patients who switched to HTD1801 saw a reduction in HbA1c of -1.3% at Week 52, substantiating the double-blind phase findings.

SYMPHONY-2 (HTD1801 as an add-on therapy to Metformin): At week 24, the reduction from baseline in HbA1c with HTD1801 (-1.2%) was superior to placebo. HbA1c reductions were sustained in patients who continued receiving HTD1801 (-1.1% at Week 52). Placebo patients who switched to HTD1801 saw a reduction in HbA1c of -1.2% at Week 52, also substantiating the double-blind phase findings.

In both studies, the durability of effect on other cardiometabolic and renal endpoints was maintained at 52 weeks, suggesting comprehensive advantages of HTD1801 beyond glycemic control with long-term treatment.

In both studies, the proportion of patients receiving HTD1801 during the double-blind phase who achieved target HbA1c<7.0% was sustained through Week 52. The lipid-lowering effects observed during the double-blind phase, including significant reductions in low-density lipoprotein cholesterol (LDL-C) and non-high-density lipoprotein cholesterol (non-HDL-C), were also maintained. Long-term HTD1801 treatment also led to continued reductions in key inflammatory biomarkers, including gamma-glutamyl transferase (GGT) and high-sensitivity C-reactive protein (hs-CRP), both associated with cardiovascular risk in patients with T2DM.

Notably, while estimated glomerular filtration rate (eGFR) remained stable in the overall population, the improvement of eGFR in patients with mild renal impairment at Week 24 was preserved at Week 52. These data highlighting the potential renal benefit of HTD1801 will be presented at a forthcoming scientific meeting.

Favorable safety and tolerability profile

Overall, long-term safety and tolerability were favorable and consistent with the double-blind phase. The types and severity of adverse events did not increase with continued HTD1801 treatment compared to newly initiated HTD1801 treatment.

About HTD1801

HTD1801 is a first-in-class new molecular entity that targets the residual risks underlying cardiovascular-kidney-metabolic (CKM) diseases. It is an orally delivered, anti-inflammatory metabolic modulator (AIMM) that, as a single molecule, exerts a unique dual mechanism of action through activation of AMP Kinase and inhibition of the NLRP3 inflammasome, two complementary pathways that mitigate metabolic dysfunction. Multiple global clinical studies have demonstrated the comprehensive benefits of HTD1801, including improved insulin sensitivity, glycemic control, lipid lowering, renal protection, weight reduction, hepatic improvement, and anti-inflammatory effects. Collectively, these findings support the potential of HTD1801 to serve as a foundation therapy in CKM disease management.

About HighTide Therapeutics

HighTide Therapeutics, Inc. (2511.HK) is a biopharmaceutical company dedicated to developing multifunctional, multi-targeted therapies for chronic metabolic diseases, with a strategic emphasis to address the residual risks of cardiovascular-kidney-metabolic (CKM) syndrome. The company focuses on delivering breakthrough treatments that generate comprehensive, multi-organ benefits for patients worldwide. HighTide has built an innovative, globally integrated pipeline of proprietary assets and advanced multiple clinical programs across chronic metabolic diseases.

The company's lead asset, HTD1801, has received two Fast Track designations and one Orphan Drug designation from the US Food and Drug Administration (FDA), and has been selected for China's *National Major Science and Technology Project for Significant New Drug Development*.

Cautionary statement required by Rule 18A.05 of the Rules Governing the Listing of Securities on The Stock Exchange of Hong Kong Limited: The Company cannot guarantee that HTD1801 will ultimately be successfully marketed. Shareholders and potential investors of the Company are advised to exercise caution when dealing in the shares of the Company.

By order of the Board
HighTide Therapeutics, Inc.
Dr. LIU Liping
Executive Director and Chief Executive Officer

Hong Kong, October 31, 2025

As at the date of this announcement, the Board comprises Dr. LIU Liping and Ms. YU Meng as executive Directors; Dr. ZHU Xun, Mr. MA Lixiong and Mr. JIANG Feng as non-executive Directors; and Mr. TAN Bo, Dr. LI Jin and Mr. HUNG Tak Wai as independent non-executive Directors.