Scilex Bio, a Controlling Interest of Joint Venture by Scilex Holding Company, Reports KDS2010 a Novel Oral Tablet Phase 2 Trial for Alzheimer's Disease (AD) Currently Enrolling with U.S. Patient Cohort to be Added in 2025

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- Currently enrolling randomized, double-blind, placebo-controlled, dose-finding, Phase 2 clinical trial to evaluate the safety and efficacy of KDS2010 in patients with Alzheimer's disease with mild cognitive impairment and mild dementia is currently recruiting in South Korea in 114 patients and U.S. cohort will be added in 2025.
- KDS2010 (Tisolagiline) is a new reversible selective monoamine oxidase B (MAO-B) inhibitor being studied for its potential in treating neurodegenerative diseases like Alzheimer's disease.
- Apart from its role as a MAO-B inhibitor, it also influences astrocytic GABA inhibition.
- In neurodegenerative diseases like Alzheimer's, altered GABAergic activity and dysfunction in astrocytic regulation of neurotransmitter systems contribute to cognitive decline and neuroinflammation.
- A highly selective and reversible MAO-B inhibitor, KDS2010 overcomes the disadvantages of the irreversible MAO-B inhibition.
- Long-term treatment with KDS2010 significantly attenuates increased astrocytic GABA levels and astrogliosis, enhances synaptic transmission, and improves learning and memory in APP/PS1 mice.[1]
- KDS2010 pharmacokinetics, lack of food effect, safety and dose selection have been characterized in Single Ascending Dose and Multiple Ascending Dose Phase 1 clinical trials with 88 healthy young adults and elderly subjects and between Korean and Western population, demonstrating favorable safety and tolerability and adequate pharmacokinetics for once-daily dosing.
- Per Health Care analyst reports 2023, Alzheimer's global drug market size is expected to rise above $15 billion by 2030 in the eight major markets, as new drugs show promise and are being launched with FDA approval to slow cognitive decline.[2]

PALO ALTO, Calif., Dec. 11, 2024 (GLOBE NEWSWIRE) -- Scilex Bio, a controlling interest of joint venture by Scilex Holding Company (Nasdaq: SCLX, "Scilex" or "Company") with IPMC Company, a representative company of the Bio Innovation Consortium ("IPMC") which holds the exclusive rights to NeuroBiogen Company's ("NB") KDS2010 global license, announced that KDS2010 (Tisolagiline) is a new reversible selective monoamine oxidase B (MAO-B) inhibitor being studied for its potential in treating neurodegenerative diseases like Alzheimer's disease (AD). Apart from its role as a MAO-B inhibitor, it also influences astrocytic GABA inhibition.

"Current treatments in development for Alzheimer's Disease are mostly injectable antibodies or peptides targeting amyloid, tau or neuroinflammation. Advancement of a small molecule with great potential to improve cognitive function that can be delivered with once-daily oral dosing holds promise for people living with Alzheimer's disease," said Richard Lipton, MD., Professor of Neurology at the Albert Einstein College of Medicine.

GABA (gamma-aminobutyric acid) is the primary inhibitory neurotransmitter in the brain, playing a key role in regulating neuronal activity and maintaining balance between excitation and inhibition. Astrocytes, a type of glial cell in the brain, have been shown to be involved in the regulation of GABA activity. In neurodegenerative diseases like Alzheimer's, altered GABAergic activity and dysfunction in astrocytic regulation of neurotransmitter systems contribute to cognitive decline and neuroinflammation. By inhibiting astrocytic GABA signaling, KDS2010 helps to reduce neuroinflammation and normalize the balance between excitatory and inhibitory signals in the brain, potentially leading to enhancing cognitive function in Alzheimer's disease.

Mechanistically, reactive astrocytes precipitate pathological hallmarks of Alzheimer's disease via hydrogen peroxide (H_2O_2) production. KDS2010 blocks MAO-B-dependent aberrant GABA/ H_2O_2 production in reactive astrocytes and eliminates neuronal inhibition, neuroinflammation, and neurodegeneration, while enhancing neuroregeneration.[3]

In the dentate gyrus of mouse models of AD, the released GABA reduces spike probability of granule cells by acting on presynaptic GABA receptors. Suppressing GABA production in reactive astrocytes restores the impaired spike probability, synaptic plasticity, and learning and memory in mice. In the postmortem brain of individuals with AD, astrocytic GABA and MAO-B are significantly upregulated. Selective inhibition of astrocytic GABA

synthesis and release is a new therapeutic strategy for treating memory impairment in AD.[4]

Clinically, short-term treatment with known irreversible MAO-B inhibitors, such as selegiline, improves cognitive deficits in AD patients, long-term treatments have shown disappointing results. Interestingly, prolonged treatment with selegiline fails to reduce aberrant astrocytic GABA levels and rescue memory impairment in APP/PS1 mice, an animal model of AD, because of increased activity in compensatory genes for a GABA-synthesizing enzyme, diamine oxidase (DAO). A highly selective and reversible MAO-B inhibitor, KDS2010 overcomes the disadvantages of the irreversible MAO-B inhibition. Long-term treatment with KDS2010 significantly attenuates increased astrocytic GABA levels and astrogliosis, enhances synaptic transmission, and improves learning and memory in APP/PS1 mice.[1]

KDS2010 pharmacokinetics, lack of food effect, safety and dose selection have been characterized in Single Ascending Dose and Multiple Ascending Dose Phase 1 clinical trials with 88 healthy young adults and elderly subjects and between Korean and Western populations, demonstrating favorable safety and tolerability and adequate pharmacokinetics for once-daily dosing. A Randomized, Double-Blind, Placebo-Controlled, Dose-Finding, Phase 2 Clinical Trial to Evaluate the Safety and Efficacy of KDS2010 in Patients with Alzheimer's Disease with Mild Cognitive Impairment and Mild Dementia is currently recruiting in South Korea in 114 patients and U.S. cohort will be added in 2025.

For more information on Scilex Holding Company, refer to www.scilexholding.com

For more information on Semnur Pharmaceuticals, refer to www.semnurpharma.com

For more information on Scilex Holding Company Sustainability Report, refer to www.scilexholding.com/investors/sustainability

For more information on ZTlido®, including Full Prescribing Information, refer to www.ztlido.com.

For more information on ELYXYB®, including Full Prescribing Information, refer to www.elyxyb.com.

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About Scilex Holding Company

Scilex Holding Company is an innovative revenue-generating company focused on acquiring, developing and commercializing the treatment for neurodegenerative and cardiometabolic diseases, and non-opioid pain management products for the treatment of acute and chronic pain. Scilex targets indications with high unmet needs and large market opportunities with non-opioid therapies for the treatment of patients with acute and chronic pain and are dedicated to advancing and improving patient outcomes. Scilex's commercial products include: (i) ZTlido ® (lidocaine topical system) 1.8%, a prescription lidocaine topical product approved by the U.S. Food and Drug Administration (the "FDA") for the relief of neuropathic pain associated with postherpetic neuralgia, which is a form of post-shingles nerve pain; (ii) ELYXYB®, a potential first-line treatment and the only FDA-approved, ready-to-use oral solution for the acute treatment of migraine, with or without aura, in adults; and (iii) Gloperba®, the first and only liquid oral version of the anti-gout medicine colchicine indicated for the prophylaxis of painful gout flares in adults.

In addition, Scilex has three product candidates: (i) SP-102 (10 mg, dexamethasone sodium phosphate viscous gel) ("SEMDEXA™" or "SP-102"), a novel, viscous gel formulation of a widely used corticosteroid for epidural injections to treat lumbosacral radicular pain, or sciatica, for which Scilex has completed a Phase 3 study and was granted Fast Track status from the FDA in 2017; (ii) SP-103 (lidocaine topical system) 5.4%, ("SP-103"), a next-generation, triple-strength formulation of ZTlido, for the treatment of acute pain and for which Scilex has recently completed a Phase 2 trial in acute low back pain. SP-103 has been granted Fast Track status from the FDA in low back pain; and (iii) SP-104 (4.5 mg, low-dose naltrexone hydrochloride delayed-release capsules) ("SP-104"), a novel low-dose delayed-release naltrexone hydrochloride being developed for the treatment of fibromyalgia, for which Phase 1 trials were completed in the second quarter of 2022.

Scilex Holding Company is headquartered in Palo Alto, California.

For more information on Scilex Holding Company, refer to www.scilexholding.com

About Semnur Pharmaceuticals, Inc.

Semnur Pharmaceuticals, Inc. ("Semnur") is a clinical-late stage specialty pharmaceutical company focused on the development and commercialization of novel non-opioid pain therapies. Semnur's lead program, SP-102 (SEMDEXA™), is the first non-opioid novel gel formulation administered epidurally in development for patients with moderate to severe chronic radicular pain/sciatica.

Semnur Pharmaceuticals, Inc. is headquartered in Palo Alto, California.

For more information on Semnur Pharmaceuticals, refer to www.semnurpharma.com

About Scilex Bio

Scilex Holding Company and IPMC Company, a representative company of the Bio Innovation Consortium ("BOIC"), which holds the exclusive rights to NeuroBiogen Company's ("NB") KDS2010 global license, formed a joint venture, Scilex Bio, to develop and commercialize a next-generation reversible MAO-B Inhibitor, a novel inhibitor of aberrant GABA production in reactive astrocytes for the treatment of obesity and neurodegenerative diseases including Alzheimer's disease.

About IPMC

IPMC is a private biopharmaceutical company focused on the development of new medicines for the treatment of cardiometabolic and neurodegenerative diseases.

Forward-Looking Statements

This press release and any statements made for and during any presentation or meeting concerning the matters discussed in this press release contain forward-looking statements related to Scilex and its subsidiaries and are subject to risks and uncertainties that could cause actual results to

differ materially from those projected. Forward-looking statements include statements regarding the Scilex and its subsidiaries, including but not limited to, statements regarding the terms of the potential licensing transaction, statements regarding KDS2010 and the potential efficacy and preclinical results, the potential for KDS2010 to be an innovative new treatment for obesity and Alzheimer's disease benefitting people living with neurodegenerative and cardiometabolic diseases, the potential market size and growth opportunity for the weight loss and Alzheimer's global drug market, the Company's outlook, goals and expectations for 2024, and the Company's development and commercialization plans. Although each of Scilex and its subsidiaries believes that it has a reasonable basis for each forward-looking statement contained in this press release, each of Scilex and its subsidiaries caution you that these statements are based on a combination of facts and factors currently known and projections of the future, which are inherently uncertain.

Risks and uncertainties that could cause actual results of Scilex to differ materially and adversely from those expressed in our forward-looking statements, include, but are not limited to: the inability of the parties to consummate the licensing transaction for any reason, including any failure to satisfy or waive any closing conditions; changes in the structure, timing and completion of the proposed transaction between Scilex and NeuroBiogen; the ability of the parties to achieve the benefits of the proposed licensing transaction, risks related to the outcome of any legal proceedings that may be instituted against the parties following the announcement of the proposed licensing transaction; risks associated with the unpredictability of trading markets; general economic, political and business conditions; the risk that the potential product candidates that Scilex or Scilex Bio develops may not progress through clinical development or receive required regulatory approvals within expected timelines or at all; risks relating to uncertainty regarding the regulatory pathway for Scilex's and Scilex Bio's product candidates; the risk that Scilex and Scilex Bio will be unable to successfully market or gain market acceptance of its product candidates; the risk that Scilex's product candidates may not be beneficial to patients or successfully commercialized; the risk that Scilex has overestimated the size of the target patient population, their willingness to try new therapies and the willingness of physicians to prescribe these therapies; risks that the outcome of the trials and studies for SP-102, SP-103 or SP-104 may not be successful or reflect positive outcomes; risks that the prior results of the clinical and investigator-initiated trials of SP-102 (SEMDEXA™), SP-103 or SP-104 may not be replicated; regulatory and intellectual property risks; and other risks and uncertainties indicated from time to time and other risks described in Scilex's most recent periodic reports filed with the SEC, including its Annual Reports on Form 10-K for the year ended December 31, 2023 and subsequent Quarterly Reports on Form 10-Q that the Company has filed or may file, including the risk factors set forth in those filings. Investors are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date of this release, and Scilex undertakes no obligation to update any forward-looking statement in this press release except as may be required by law.

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