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NewsRelease

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Sunovion and PsychoGenics Announce Positive Results from Pivotal Phase 2 Study of Novel Investigational Agent SEP-363856 for the Treatment of Schizophrenia

— SEP-363856 was identified through a collaboration between Sunovion and PsychoGenics —
— Findings provide validation of the PsychoGenics discovery platform —
— SEP-363856 holds promise to be the first agent for the treatment of schizophrenia that does not bind to dopamine 2 (D2) receptors —

Marlborough, Mass., and Paramus NJ, December 13, 2018 – Sunovion Pharmaceuticals Inc. (Sunovion) and PsychoGenics Inc. (PsychoGenics), today announced that positive results from SEP 361-201, a pivotal Phase 2 study that evaluated the efficacy and safety of SEP-363856, a novel psychotropic agent for the treatment of patients with schizophrenia, were presented at the 57th Annual Meeting of the American College of Neuropsychopharmacology (ACNP) in Hollywood, Fla.

The study met its primary endpoint, demonstrating that hospitalized patients with acute exacerbation (worsening) of schizophrenia treated with SEP-363856 showed statistically significant and clinically meaningful improvement in the Positive and Negative Syndrome Scale (PANSS) total score compared to placebo after four weeks of treatment (-17.2 vs. -9.7, respectively; p=0.001). Patients treated with SEP-363856 also showed improvement in the overall severity of illness as assessed by the Clinical Global Impression Scale - Severity (CGI-S) (p<0.001). In addition, improvement was found in all major PANSS (positive, negative and general psychopathology) subscales (p<0.02).

“For more than 60 years, the treatment of schizophrenia has focused on blocking dopamine receptors. Finding a schizophrenia medication that works outside of a direct action on the dopamine system would be highly desirable, and SEP-363856 may represent such a breakthrough. The results of the Phase 2 trial are consistent in showing improvement in positive and negative symptoms, without the traditional side effects associated with dopamine blockers,” said Shitij Kapur, M.B.B.S, Ph.D.,

F.R.C.P.C., F.Med.Sci., Dean Faculty of Medicine, Dentistry and Health Sciences, University of Melbourne. “The results need to be replicated in further studies and broader populations, but, if these results hold, it could be a remarkable advance for patients and health care providers, as well as a great new avenue for exploration of new scientific mechanisms for psychotic disorders.”

SEP-363856 was found to be generally well tolerated with notable similarities to placebo treatment in discontinuation rates; proportion of patients experiencing extrapyramidal symptoms or akathisia; and change in metabolic parameters such as weight, lipids, glucose and prolactin.

SEP-363856 does not bind to D2 or other dopaminergic receptors or to serotonergic receptors (except for 5-HT1A), which are thought to mediate the effects of currently available antipsychotic medicines. Although the exact mechanism of action is unknown, SEP-363856 is believed to activate TAAR1 (trace amine-associated receptor 1) in addition to 5-HT1A (serotonin 1A) receptors.

“The results of this first placebo-controlled study assessing the utility of SEP-363856 in patients with schizophrenia are exciting, and we intend to advance the development of this novel investigational medicine as quickly as possible,” said Antony Loebel, M.D., Executive Vice President and Chief Medical Officer at Sunovion, Head of Global Clinical Development for Sumitomo Dainippon Pharma Group. “As a part of our commitment to developing new treatments for major unmet needs in neuropsychiatry, Sunovion has taken a novel approach to the discovery of new psychotropic agents. We are very pleased that SEP-363856, the most advanced molecule derived from our PsychoGenics collaboration, has shown such strong results for patients with schizophrenia.”

“We believe that the results from this study illustrate the promise of the PsychoGenics’ target-agnostic approach using the SmartCube® platform,” said Eric Nestler, M.D., Ph.D., Director of the Friedman Brain Institute at the Icahn School of Medicine at Mount Sinai and Chairman of the PsychoGenics Scientific Advisory Board. “We look forward to continuing our work with Sunovion in identifying compounds that have the potential to make a significant difference for patients.”

Sunovion’s clinical-stage pipeline in neuropsychiatry includes several additional compounds that were discovered using the PsychoGenics SmartCube® platform together with other novel systems biology approaches.

Detailed Study Results (SEP 361-201)

SEP 361-201 was a four-week, double-blind, placebo controlled multiregional study that randomized 245 hospitalized patients with acute exacerbation of schizophrenia to once daily treatment with flexibly-dosed SEP-363856 (50mg or 75mg) or placebo (1:1). The primary efficacy endpoint was the change from baseline in Positive and Negative Syndrome Scale (PANSS) total score at Week Four for SEP-363856 versus placebo, assessed using a mixed model for repeated measures analysis.

The study met its primary endpoint, demonstrating statistically significant and clinically meaningful improvement in the Positive and Negative Syndrome Scale (PANSS) total score compared to placebo after four weeks of treatment (-17.2 vs. -9.7; p=0.001; effect size, 0.45).

Secondary efficacy assessments that compared SEP-363856 versus placebo support the findings of the primary endpoint including change from baseline to Week Four in the Clinical Global Impressions-Severity (CGI-S) score (-1.0 vs. -0.5; p<0.001), PANSS positive subscale score (-5.5 vs. -3.9; p=0.019), PANSS negative subscale score (-3.1 vs. -1.6; p=0.008), PANSS general psychopathology subscale score (-9.0 vs. -4.7; p<0.001).

Safety and tolerability of SEP-363856 were assessed throughout the study. The overall discontinuation rate was comparable for SEP-363856 and placebo (21.7 percent and 20.8 percent, respectively) and for rate of discontinuations due to an adverse event (8.3 percent and 6.4 percent, respectively). Adverse events occurring in at least two percent of patients and in the SEP-363856 group (with the higher incidence in the SEP-363856 group), included somnolence (6.7 percent and 4.8 percent), agitation (5.0 percent and 4.8 percent), nausea (5.0 percent and 3.2 percent), diarrhea (2.5 percent and 0.8 percent) and dyspepsia (2.5 percent and 0.0 percent). Additionally, change in weight, lipids, glucose and prolactin associated with SEP-363856 treatment was similar to placebo during the study. The proportion of patients who experienced extrapyramidal symptoms treated with SEP-363856 and placebo was 3.3 and 3.2 percent, respectively.

This study, which was designed, conducted and supported by Sunovion Pharmaceuticals, is part of a global development program for SEP-363856, a novel investigational psychotropic agent being studied as a treatment for patients with schizophrenia or Parkinson's disease psychosis. Patients who completed Study 361-201 were eligible to continue in an open label, long-term extension study which is currently ongoing.

About SEP-363856

SEP-363856 is a psychotropic agent with a novel, non-D2 mechanism of action, distinct from currently marketed antipsychotics. Sunovion discovered SEP-363856 in collaboration with PsychoGenics based in part on a mechanism-independent approach using the in vivo phenotypic SmartCube® platform and associated artificial intelligence algorithms. SEP-363856 was optimized for antipsychotic activity by Sunovion medicinal chemists based on quantitative structure-activity relationship analysis, in collaboration with PsychoGenics. SEP-363856 is jointly owned by Sunovion and PsychoGenics. Sunovion has exclusive rights to develop and commercialize SEP-363856 globally.

SEP-363856 is being studied in a global development program for schizophrenia as well as for Parkinson’s disease psychosis, with additional indications under consideration. Clinical trial results to date demonstrate a predictable pharmacokinetic (PK) profile suitable for once daily use.

About Schizophrenia

Schizophrenia is a chronic, serious and often severely disabling brain disorder that affects more than 23 million people worldwide[1] and approximately one in 100 adults (about 2.4 million people) in the United States.[2] It is characterized by positive symptoms, such as hallucinations, delusions and disorganized thinking as well as negative symptoms, such as lack of emotion, social withdrawal, lack of spontaneity and cognitive impairment that includes problems with memory, attention and the ability to plan, organize and make decisions.[3]

About Sunovion Pharmaceuticals Inc. (Sunovion)

Sunovion is a global biopharmaceutical company focused on the innovative application of science and medicine to help people with serious medical conditions. Sunovion's vision is to lead the way to a healthier world. The company's spirit of innovation is driven by the conviction that scientific excellence paired with meaningful advocacy and relevant education can improve lives. With patients at the center of everything it does, Sunovion has charted new paths to life-transforming treatments that reflect ongoing investments in research and development and an unwavering commitment to support people with psychiatric, neurological and respiratory conditions.

Headquartered in Marlborough, Mass., Sunovion is an indirect, wholly-owned subsidiary of Sumitomo Dainippon Pharma Co., Ltd. Sunovion Pharmaceuticals Europe Ltd., based in London, England, and Sunovion Pharmaceuticals Canada Inc., based in Mississauga, Ontario, are wholly-owned direct subsidiaries of Sunovion Pharmaceuticals Inc. Additional information can be found on the company's websites: www.sunovion.com, www.sunovion.eu and www.sunovion.ca. Connect with Sunovion on Twitter, LinkedIn, Facebook and YouTube.

About PGI Drug Discovery LLC and PsychoGenics Inc. (collectively PsychoGenics)

PsychoGenics Inc. and its discovery arm PGI Drug Discovery LLC (collectively known as PsychoGenics) have pioneered the translation of rodent behavioral and physiological responses into robust, high-throughput and high-content phenotyping. PsychoGenics' drug discovery platforms, SmartCube®, NeuroCube® and PhenoCube®, have been used in shared-risk partnerships with major pharmaceutical companies, resulting in the discovery of several novel compounds now in clinical trials or advanced preclinical development.

PsychoGenics' capabilities also include standard behavioral testing, electrophysiology, translational electroencephalogram (EEG), molecular biology, microdialysis and quantitative immunohistochemistry. In addition, the company offers a variety of in-licensed transgenic mouse models that support research in areas such as Huntington's disease, autism spectrum disorders, psychosis/schizophrenia, depression/ post-traumatic stress disorder (PTSD), Alzheimer's disease, Parkinson's disease, muscular dystrophy, amyotrophic lateral sclerosis (ALS) and seizure disorders. For more information on PsychoGenics Inc., visit www.psychogenics.com.

About Sumitomo Dainippon Pharma Co., Ltd.

Sumitomo Dainippon Pharma is among the top-ten listed pharmaceutical companies in Japan, operating globally in major pharmaceutical markets, including Japan, the U.S., China and the European Union. Sumitomo Dainippon Pharma aims to create innovative pharmaceutical products in the Psychiatry & Neurology area, the Oncology area and Regenerative medicine/Cell therapy field, which have been designated as the focus therapeutic areas. Sumitomo Dainippon Pharma is based on the merger in 2005 between Dainippon Pharmaceutical Co., Ltd., and Sumitomo Pharmaceuticals Co., Ltd. Today, Sumitomo Dainippon Pharma has more than 6,000 employees worldwide. Additional information about Sumitomo Dainippon Pharma is available through its corporate website at https://www.ds-pharma.com.

For a copy of this release, visit Sunovion's web site at www.sunovion.com

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