

FOR IMMEDIATE RELEASE



**SHIONOGI INC. ANNOUNCES COMMERCIAL AVAILABILITY OF  
KAPVAY™ (clonidine hydrochloride) EXTENDED-RELEASE TABLETS  
FOR THE TREATMENT OF ADHD**

**FLORHAM PARK, NJ (January 10, 2011)** – Shionogi Inc., the U.S.-based group company of Shionogi & Co., Ltd., today announced a true milestone as it marks the first commercial availability for the non-central nervous system stimulant medication KAPVAY™, an extended-release oral formulation of clonidine for Attention Deficit Hyperactivity Disorder (ADHD) in children and adolescents. KAPVAY™ is the first and only FDA-approved ADHD treatment indicated for use as add-on therapy to stimulant medication, in addition to use as monotherapy.

“Shionogi is extremely proud to bring KAPVAY™ to market in the U.S.,” said Donald C. Manning, MD, PhD, Chief Medical Officer of Shionogi Inc. “The extended-release version of clonidine hydrochloride found in KAPVAY™ offers an exciting new treatment option for children and adolescents with ADHD who are not experiencing adequate symptom relief from stimulants alone.”

ADHD affects more than 4.5 million children in the U.S., with at least 7 percent of U.S. school-aged children believed to suffer from the condition. Symptoms include difficulty in maintaining attention and focus and in controlling behavior, as well as hyperactivity/over-activity. While stimulant medications remain a first line treatment for ADHD, up to 30 percent of ADHD patients do not achieve an optimal response to stimulant monotherapy.

KAPVAY™’s recent FDA approval was based on two Phase III studies, which demonstrated significant efficacy at Week 5 in children and adolescents (6-17 years) with ADHD treated with KAPVAY™. Signs and symptoms of ADHD were evaluated using the investigator administered and scored ADHD Rating Scale-IV-Parent Version (ADHDRS-IV) total score, including hyperactive/impulsivity and inattentive subscales. Treatment-emergent adverse events, such as somnolence and fatigue, were mostly mild to moderate. Thirteen percent (13%) of patients receiving KAPVAY™ discontinued from the pediatric monotherapy study due to adverse reactions. In the pediatric adjunctive treatment to stimulants study, one patient out of 102 discontinued from KAPVAY™.

“There is a portion of children and adolescents who suffer from symptoms of ADHD who are not responding optimally to current therapies,” said Rakesh Jain, MD, MPH, Assistant Clinical Professor, Department of Psychiatry, Texas Tech University School of Medicine – Permian Basin, Midland, Texas and Director of Psychiatric Drug Research for R/D Clinical Research at Lake Jackson, Texas, and one of the investigators in the clinical trials. “The availability of an extended-release formulation of clonidine hydrochloride is an important addition to the current ADHD treatment landscape.”

**About KAPVAY™**

KAPVAY™ (clonidine hydrochloride) extended-release is indicated for the treatment of ADHD as monotherapy and as adjunctive therapy to stimulant medications. The efficacy of KAPVAY™ in the treatment of ADHD is based on two controlled trials (one monotherapy and one adjunctive to stimulant medication) in children and adolescents ages 6-17 who met DSM-IV criteria for ADHD hyperactive or

combined hyperactive/inattentive subtypes. KAPVAY™ is indicated as an integral part of a total treatment program for ADHD that may include other measures (psychological, educational, and social) for patients with this syndrome. The effectiveness of KAPVAY™ for longer-term use (more than 5 weeks) has not been systemically evaluated in controlled trials.

Administered orally, KAPVAY™ exerts its pharmacological effects as a centrally acting alpha2-adrenoceptor agonist. The formulation in KAPVAY™ is designed to delay the absorption of active drug in order to decrease peak to trough plasma concentration differences.

### **Important Safety Information**

KAPVAY™ should not be used in patients with known hypersensitivity to clonidine.

KAPVAY™ can cause dose-related decreases in blood pressure and heart rate, use caution in treating patients who have a history of syncope or may have a condition that predisposes them to syncope, such as hypotension, orthostatic hypotension, bradycardia, or dehydration. Use with caution in patients treated concomitantly with antihypertensives or other drugs that can reduce blood pressure or heart rate or increase the risk of syncope.

Somnolence/sedation were commonly reported adverse reactions in clinical studies with KAPVAY™. Potential for additive sedative effects with central nervous system (CNS) depressant drugs, advise patients to avoid use with alcohol. Caution patients against operating heavy equipment or driving until they know how they respond to KAPVAY™.

Patients should be instructed not to discontinue KAPVAY™ therapy without consulting their physician due to the potential risk of withdrawal effects. KAPVAY™ should be discontinued slowly in decrements of no more than 0.1 mg every 3 to 7 days.

In patients who have developed localized contact sensitization or other allergic reaction to clonidine in a transdermal system, substitution of oral clonidine hydrochloride therapy may be associated with the development of a generalized skin rash, urticaria, or angioedema.

Use cautiously in patients with vascular disease, cardiac conduction disease, or chronic renal failure: Monitor carefully and uptitrate slowly.

Clonidine may potentiate the CNS-depressive effects of alcohol, barbiturates or other sedating drugs. Use caution when KAPVAY™ is administered concomitantly with antihypertensive drugs, due to the additive pharmacodynamics effects (e.g. hypotension, syncope).

KAPVAY™ should not be used during pregnancy unless clearly needed. Since clonidine hydrochloride is excreted in human milk, caution should be exercised when KAPVAY™ is administered to a nursing woman.

Caution is warranted in patients receiving clonidine concomitantly with agents known to affect sinus node function or AV nodal conduction (e.g., digitalis, calcium channel blockers and beta-blockers) due to a potential for additive effects such as bradycardia and AV block.

Clonidine, the active ingredient in KAPVAY™, is also approved as an antihypertensive. Do not use KAPVAY™ in patients concomitantly taking other clonidine-containing products, (e.g. Catapres®, JENLOGA, etc.).

Common adverse reactions (incidence at least 5% and twice the rate of placebo) include: Somnolence, fatigue, upper respiratory tract infection, irritability, throat pain, insomnia, nightmares, emotional disorder, constipation, nasal congestion, increased body temperature, dry mouth, and ear pain.

To report SUSPECTED ADVERSE REACTIONS, contact Shionogi Pharma, Inc. at 1-800-849-9707 ext. 1454 or FDA at 1-800-FDA-1088 or [www.fda.gov/medwatch](http://www.fda.gov/medwatch).

For full prescribing information, please visit [www.KAPVAY.com](http://www.KAPVAY.com).

### **About ADHD**

ADHD is a neurobehavioral disorder that most often occurs in childhood and may continue into adolescence and adulthood. There are three subtypes of ADHD: predominantly hyperactive-impulsive, predominantly inattentive, and combined hyperactive-impulsive and inattentive, with the latter being the most common. ADHD symptoms fall under three main categories: inattention, hyperactivity and impulsivity, which can include behaviors such as trouble focusing, frequent daydreaming, excessive talking, fidgeting/squirming, chronic impatience and difficulty waiting their turn, depending on the category.

The cause of ADHD is not yet known. However, research has shown potential links to genetic and environmental factors. While there is no cure for ADHD, the disorder can be managed with a variety of treatments including parental education and training, behavioral therapy and prescription medication.

### **About Shionogi & Co., Ltd.**

Headquartered in Osaka, Japan, Shionogi & Co., Ltd. is a major research-driven pharmaceutical company dedicated to placing the highest value on patients. Shionogi's Research and Development currently targets three therapeutic areas: Infectious Diseases, Pain, and Metabolic Syndrome. The Company has provided such innovative medicines as Crestor and Doripenem, which have been successfully delivered to millions of patients. In addition, Shionogi is engaged in new research areas such as allergy and cancer. Contributing to the health of patients around the world through development in these therapeutic areas is Shionogi's primary goal. For more details, please visit [www.shionogi.co.jp](http://www.shionogi.co.jp). For more information on Shionogi Inc., headquartered in Florham Park, NJ, please visit [www.shionogi-inc.com](http://www.shionogi-inc.com).

### **Forward Looking Statements**

*This announcement contains forward-looking statements. These statements are based on expectations in light of the information currently available, assumptions that are subject to risks and uncertainties which could cause actual results to differ materially from these statements. Risks and uncertainties include general domestic and international economic conditions such as general industry and market conditions, and changes of interest rate and currency exchange rate. These risks and uncertainties particularly apply with respect to product-related forward-looking statements. Product risks and uncertainties include, but are not limited to, completion and discontinuation of clinical trials; obtaining regulatory approvals; claims and concerns about product safety and efficacy; technological advances; adverse outcome of important litigation; domestic and foreign healthcare reforms and changes of laws and regulations. Also for existing products, there are manufacturing and marketing risks, which include, but are not limited to, inability to build production capacity to meet demand, unavailability of raw materials and entry of competitive products. The company disclaims any intention or obligation to update or revise any forward-looking statements whether as a result of new information, future events or otherwise.*

Contact:

Shionogi Inc.

Yoshimasa Kyokawa

Telephone: +1-973-966-6900

[ykyokawa@shionogi-inc.com](mailto:ykyokawa@shionogi-inc.com)

HealthStar Public Relations

Dave Schemelia

Telephone: +1-609-468-9325

[dschemelia@healthstarpr.com](mailto:dschemelia@healthstarpr.com)

# # #