11960 Southwest 144th Street
Miami, Florida 33186
305-253-1916 ▼ Toll-Free: 888-253-5099
www.noven.com

A Member of the Hisamitsu Group

PRESS RELEASE

NOVEN TO PRESENT DATA FOR: EXTRAPOLATING PEDIATRIC TRANSDERMAL ADHD TREATMENT EFFICACY DATA TO ADULT POPULATIONS AND CORRELATING TREATMENT EFFECT DURATION WITH PATCH WEAR TIMES AT AMERICAN PSYCHIATRIC NURSES ASSOCIATION ANNUAL CONFERENCE

– First study extrapolates efficacy of transdermal dextroamphetamine from pediatric to adult populations–

–Second study explores variations in patch wear-times–

October 17, 2022 – Miami, FL and Jersey City, NJ – Noven Pharmaceuticals. Inc., (Noven), a wholly owned subsidiary of Hisamitsu Pharmaceutical Co., Inc. focusing on the development of transdermal therapy, announced today it will present the results of two pharmacokinetic (PK) modeling datasets at the 36th American Psychiatric Nurses Association (APNA) annual conference in Long Beach, California October 19-22, 2022. The data discusses the investigation of variable wear times for the dextroamphetamine transdermal system (d-ATS) for the treatment of Attention-Deficit/Hyperactivity Disorder (ADHD) and extrapolation of efficacy of d-ATS from pediatric and adolescent patients to adults respectively.

In the "Investigation of Variable Wear Times for the d-ATS System Using Population Pharmacokinetic-Pharmacodynamic Modeling", a population PK model was developed to describe amphetamine disposition following d-ATS administration. To characterize the onset and duration of effect after d-ATS administration, this model was used to construct a population PK/PD model utilizing SKAMP total score data from the following two pediatric clinical studies:

- PK/PD clinical pharmacology study (single-dose, open-label) in children 6-12 years of age with ADHD
- Randomized, double-blind, placebo-controlled efficacy and safety study in children and adolescents 6-17 years of age with ADHD

The d-ATS exposure-response relationship and potential impact of d-ATS wear time (4-9 hours) under different assumptions for amphetamine absorption post-removal were explored through simulation.

“Based on these results, our d-ATS treatment will give our patients a new option for ADHD symptom management,” said presenter Kanan Balakrishnan, Pharm.D., Executive Director of Regulatory Affairs, Product Development at Noven.

Similarities in pathophysiology, disease state characteristics, and treatment outcomes between pediatric and adult ADHD patients have been demonstrated. Furthermore, post-marketing experience and published evidence support a tight link between the pharmacodynamic effects of amphetamines (AMP) and their pharmacokinetic (PK) profile in attention-deficit/hyperactivity disorder (ADHD). In the research, “Extrapolation of the Efficacy of a Dextroamphetamine Transdermal System Investigated in Pediatric Populations to Adults Using Pharmacokinetic Modeling” the established d-ATS PK model was used to simulate exposures at the doses tested in the pivotal pediatric study (ATS 5mg/9hours, 10mg/9hours, 15mg/9hours and 20mg/9hours equivalent to the approved XELSTRYM 4.5mg/9hours,

9mg/9hours, 13.5mg/9hours and, 18mg/9hours dose, respectively) and compare them to adult exposures at the same doses.

The simulated data demonstrated that amphetamine disposition was comparable for adult and pediatric ADHD populations after accounting for body size effects and that 20-mg d-ATS (equivalent to the XELSTRYM 18mg/9hour dose strength) in adults produced exposures comparable to 15-mg d-ATS (equivalent to the approved XELSTRYM 13.5mg/9hour dose strength) in pediatric patients, the dose demonstrated as efficacious and deemed optimal in the pivotal study.

"The comparable d-ATS exposures and pharmacokinetic profile across patient populations supports the extrapolation of efficacy findings from pediatrics to adults demonstrating that adults are likely to yield efficacy and safety results similar to those observed in the pivotal pediatric trial" said presenter Mariacristina Castelli, M.D., Chief Clinical and Regulatory Officer at Noven. "This is an important step in showcasing that efficacy data for d-ATS can apply across age groups."

Time and location for each presentation is listed below:

- Poster Title: Extrapolation of the Efficacy of a Dextroamphetamine Transdermal System Investigated in Pediatric Populations to Adults Using Pharmacokinetic Modeling
- Open to View:
    - Thursday, October 20th from 10:00 AM – 6:30 PM PT / 1:00 PM – 9:30 PM ET
    - Friday, October 21st from 10:00 AM – 3:00 PM PT / 1:00 PM – 6:00 PM ET
- Presenter Interaction: Friday, October 21st from 10:30 AM – 11:30 AM PT / 1:30 PM – 2:30 PM ET
- Poster: 154

- Poster Title: Population Pharmacokinetic-Pharmacodynamic Modeling of Variable Wear Times for a Dextroamphetamine Transdermal System
- Open to View:
    - Thursday, October 20th from 10:00 AM – 6:30 PM PT / 1:00 PM – 9:30 PM ET
    - Friday, October 21st from 10:00 AM – 3:00 PM PT / 1:00 PM – 6:00 PM ET
- Presenter Interaction: Friday, October 21st from 10:30 AM – 11:30 AM PT / 1:30 PM – 2:30 PM ET
- Poster: 153

"As the developers of the first amphetamine transdermal patch approved for ADHD in the U.S., we are pleased to offer the ADHD community a treatment that will allow clinicians, alongside their patients, to individualize their treatment experience,[1]" said Joel Lippman, M.D., Chief Operating Officer and Chief Medical Officer at Noven. "We wanted our product to reflect that when it comes to treating patients with ADHD, there isn't a one-size-fits-all solution."

Approved this year by the FDA for Adults and Children with ADHD six years' age and older, Noven's d-ATS system will be available in 2023 for prescription under the brand name XELSTRYM™.

To learn more about XELSTRYM and stay abreast of the latest news and updates, register at https://www.xelstrym.com/.

[1] XELSTRYM™ should be removed within nine hours after application. Dose titration and final dosage should be individualized depending on clinical response and tolerability

About Attention Deficit Hyperactivity Disorder (ADHD)

ADHD is one of the most common neurodevelopmental disorders of childhood. It is usually first diagnosed in childhood and often lasts into adulthood. Children with ADHD may have trouble paying attention, controlling impulsive behaviors (may act without thinking about what the result will be), or be overly active. ADHD can last into adulthood. Some adults have ADHD but have never been diagnosed. The symptoms can cause difficulty at work, at home, or with relationships. Symptoms can become more severe when the demands of adulthood increase and may look different at older ages, for example, hyperactivity may appear as extreme restlessness.

About XELSTRYM™

XELSTRYM is the first and only FDA-approved, once-daily amphetamine transdermal patch for the treatment of Attention-Deficit/Hyperactivity Disorder (ADHD) in adults and pediatric patients 6 years and older. XELSTRYM should be applied 2 hours before an effect is needed and removed within 9 hours after application.

IMPORTANT SAFETY INFORMATION

What is XELSTRYM?

XELSTRYM is a central nervous system stimulant prescription medicine used for the treatment of Attention-Deficit/Hyperactivity Disorder (ADHD) in adults and children 6 years and older. It is not known if XELSTRYM is safe and effective in children younger than 6 years of age.

IMPORTANT SAFETY INFORMATION

Abuse and dependence: XELSTRYM, other amphetamine-containing medicines, and methylphenidate have a high chance for abuse and can cause physical and psychological dependence. Your healthcare provider (HCP) should check you or your child for signs of abuse and dependence before and during treatment with XELSTRYM.

- Tell your HCP if you or your child has ever abused or been dependent on alcohol, prescription medicines or street drugs.
- Your HCP can tell you how physical and psychological dependence and drug addiction are different**.**

XELSTRYM is a federally controlled substance (CII) because it contains amphetamine that can be a target for people who abuse prescription medicines or street drugs. Keep XELSTRYM in a safe place to protect it from theft. Never sell or give your XELSTRYM to anyone else because it may cause death or harm to them and it is against the law.

Do not use XELSTRYM if you or your child are:

- Allergic to amphetamine or any of the ingredients in XELSTRYM. See the end of the Medication Guide for a complete list of ingredients in XELSTRYM.
- Taking or have taken within the past 14 days a medicine called a monoamine oxidase inhibitor (MAOI), including the antibiotic linezolid or the intravenous medicine called methylene blue.

XELSTRYM can cause serious side effects, including:

- **Heart-related problems, including:**
    - sudden death, stroke, and heart attack in adults
    - sudden death in children who have heart problems or heart defects
    - increased blood pressure and heart rate

Your HCP should check you or your child carefully for heart problems before starting treatment with XELSTRYM. Tell your HCP if you or your child have any heart problems, heart defects, high blood pressure, or a family history of these problems. Your HCP should check your or your child's blood pressure and heart rate regularly during treatment with XELSTRYM. **Call your HCP or go to the nearest hospital emergency room right away if you or your child have any signs of heart problems such as chest pain, shortness of breath, or fainting during treatment with XELSTRYM.**

- **Mental (psychiatric) problems, including:** new or worse behavior and thought problems, new or worse bipolar illness, new psychotic symptoms (such as hearing voices, or seeing or believing things that are not real) or new manic symptoms. Tell your HCP about any mental problems you or your child have or about a family history of suicide, bipolar illness, or depression. **Call your HCP right away if you or your child have any new or worsening mental symptoms or problems during treatment with XELSTRYM, especially hearing, seeing or believing things that are not real, or new manic symptoms.**
- **Slowing of growth (height or weight) in children**. Children should have their height and weight checked often while on XELSTRYM. Your HCP may stop treatment with XELSTRYM if your child is not growing or gaining height or weight as expected.
- **Circulation problems in fingers and toes (peripheral vasculopathy, including Raynaud's phenomenon):** fingers or toes may feel numb, cool, painful, fingers or toes may change color from pale, to blue, to red. Tell your HCP if you or your child has any numbness, pain, skin color change, or sensitivity to temperature in your fingers or toes.
  Call your HCP right away if you or your child have any signs of unexplained wounds appearing on fingers or toes while using XELSTRYM.
- **Serotonin syndrome:** symptoms such as agitation, fast heartbeat, flushing, seizures, coma, sweating, loss of coordination, confusion, dizziness, tremors, stiff muscles, muscle twitching, seeing or hearing things that are not real (hallucinations), changes in blood pressure, high body temperature (hyperthermia), nausea, vomiting, or diarrhea may occur
  Stop using XELSTRYM and call your HCP or go to the emergency room if symptoms occur. Serotonin syndrome may occur if XELSTRYM is taken with certain medicines and may be life-threatening.
- **Allergic skin rash (contact sensitization)**: Stop using XELSTRYM and tell your HCP right away if you or your child develop swelling or blisters at or around the application site.
- **Application site reactions** have happened while wearing XELSTRYM and after removal of the patch. Symptoms include pain, itching, burning feeling, redness, discomfort, or swelling at the application site. Call your HCP if you or child develop any application site reactions that do not resolve on their own.

Before taking XELSTRYM tell your healthcare provider if you:

- Are pregnant or plan to become pregnant. It is not known if XELSTRYM may harm your unborn baby.
- Are breastfeeding or plan to breastfeed. XELSTRYM can pass into your milk. Do not breastfeed while taking XELSTRYM. Talk to your doctor about the best way to feed your baby if you take XELSTRYM.

What should I avoid while using XELSTRYM?

- Do not drive, operate heavy machinery, or do other potentially dangerous activities until you know how XELSTRYM affects you.
- Avoid exposing the application site to direct external heat sources such as hair dryers, heating pads, electric blankets, heat lamps, saunas, hot tubs, and heated water beds as exposure to heat can cause too much medicine to pass into your body and cause serious side effects.

What are the possible side effects of XELSTRYM?

- The most common side effects of XELSTRYM include:
    - decreased appetite
    - headache
    - trouble sleeping
    - stomach pain
    - nausea
    - increased blood pressure
    - muscle twitching (tics)
    - vomiting
    - irritability
    - increased heart rate

Please read the Medication Guide and Full Prescribing Information including the Boxed Warning.

To report suspected Adverse Reactions, contact Noven at 1-800-455-8070 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

There is a pregnancy registry for women who are exposed to XELSTRYM during pregnancy. The purpose of the registry is to collect information about the health of women exposed to XELSTRYM and their baby. If you or your child becomes pregnant during treatment with XELSTRYM, talk to your HCP about registering with the National Pregnancy Registry for Psychiatric Medications at 1-866-961-2388 or visit online at https://womensmentalhealth.org/clinical-and-research-programs/pregnancyregistry/othermedications/

XEL-5008-16 (2.0)

10/2022

About Noven Pharmaceuticals, Inc.

Noven Pharmaceuticals, Inc. is a specialty pharmaceutical company engaged in the research, development, manufacturing, marketing and sale of prescription pharmaceutical products. Noven's mission is to develop and offer pharmaceutical products that meaningfully benefit patients around the world, with a commitment to advancing patient care through transdermal drug delivery. Noven is a standalone operating subsidiary of Japan-based Hisamitsu Pharmaceutical Co., Inc., serving as Hisamitsu's U.S. platform for prescription pharmaceuticals, and helping Hisamitsu bring the benefits of patch therapy to the world. For more information about Noven, visit http://www.noven.com. For information about Hisamitsu, visit https://global.hisamitsu.

Contact:
Natalie Andrade
Manager – Communications
305-282-7950
CorporateAffairs@noven.com