Sunovion Announces Results of Health Outcomes Analyses Supporting the Use of Aptiom® (eslicarbazepine acetate) in People with Partial-Onset Seizures at the 68th American Academy of Neurology (AAN) Annual Meeting

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Survey data compares antiepileptic drug preferences for neurologists and people with epilepsy

MARLBOROUGH, Mass.--(BUSINESS WIRE)--Sunovion Pharmaceuticals Inc. (Sunovion) today announced results of Health Economics and Outcomes Research (HEOR) analyses reinforcing the use of Aptiom™ (eslicarbazepine acetate) as monotherapy or adjunctive therapy for partial-onset seizures at the 68th American Academy of Neurology (AAN) Annual Meeting in Vancouver, Canada. Additional results from a national survey quantified the impact of antiepileptic drug (AED) attributes on physician prescribing and the preferences of people with epilepsy. Data will be shared through multiple poster presentations at AAN.

"Epilepsy can be a challenging condition to manage, and we’re committed to providing health outcomes information that supports people with partial-onset seizures," said Kritika Rajagopalan, Head of Global Health Economics and Outcomes Research, Sunovion. "The studies presented at AAN reinforce the role of APTIOM as a treatment option for people living with partial-onset seizures.

Assessment of Eslicarbazepine Acetate Monotherapy vs. Other Anti-Epileptic Drugs for Refractory Partial-Onset Seizures: Results of a Network Meta-Analysis Using Historical-Control Trials (Poster 2.023, Presented Sunday, April 17, 2016, 8:30 a.m.)

A systematic review and network meta-analysis among monotherapy AEDs found that APTIOM had the lowest odds of study exit due to meeting pre-specified criteria indicating worsening of seizure control, and the lowest odds of study discontinuation for all other reasons, compared to all evaluated AEDs.

Methodology and Results
Exit rates and all-cause discontinuations among monotherapy AEDs for refractory partial-onset seizures were compared through a systematic review. Six historical-control studies were identified and evaluated based on a pre-specified protocol. A statistically significant lower likelihood of study exit was observed for each AED versus historical controls (odds ratio [95 percent confidence interval (CI)] - APTIOM: 0.05 (0.02 to 0.17); lamotrigine XR: 0.07 (0.02 to 0.26); levetiracetam: 0.08 (0.02 to 0.27); pregabalin: 0.09 (0.02 to 0.34); levetiracetam XR: 0.11 (0.03 to 0.36). Similar results were obtained for discontinuations in the double-blind phase of the study, except for pregabalin which showed higher likelihood of discontinuations [odds ratio (95 percent CI): 0.48 (0.1 to 2.26)] and for all-cause discontinuation [odd ratio (95 percent CI): 0.47 (0.1 to 2.15)].

Patients Treated with Eslicarbazepine Acetate Monotherapy Show Quality of Life Improvement (Poster 2.028, Presented Sunday, April 17, 2016, 8:30 a.m.)

In a pooled analysis of two historical-controlled APTIOM Phase 3 studies (093-045 and 093-046), patients treated with APTIOM monotherapy, who either completed the trial or responded to treatment, experienced significant improvements in their health-related quality-of-life, with many experiencing clinically meaningful improvement.

Methodology and Results
Changes in health-related quality of life were evaluated among Completers (n=226; patients who converted to APTIOM monotherapy and completed the study), and Responders (n=134; patients who achieved a seizure frequency reduction greater than or equal to 50 percent), using the Quality of Life in Epilepsy-31 (QOLE-31) questionnaire. The QOLE-31 is an instrument that assesses daily functioning and overall well-being in patients with epilepsy. The mean change in QOLE-31 Total Score and seven subscale scores (Seizure Worry, Emotional Well-Being, Energy/Fatigue, Cognitive Functioning, Medication Effects, Social Functioning, Overall Quality of Life) from baseline to Week 18 were compared to standard minimal clinically-important difference (MCID) change scores. Results showed the mean change in QOLE-31 Total Score was significantly improved and exceeded the MCID of 5.19 among Completers (mean change was 6.72, p<0.001) and Responders (mean change was 7.71, p<0.001). Significant improvements in all seven subscale scores were observed among Completers (p<0.001) and Responders (p<0.05), and all exceeded the MCID, except for Energy/Fatigue among Responders, and Emotional Well-Being among both Completers and Responders.

Eslicarbazepine Acetate Associated with Reduced Seizure Severity in Addition to Reduced Seizure Frequency (Poster 2.031, Presented Sunday, April 17, 2016, 8:30 a.m.)

A post-hoc analysis of the Phase 3, randomized, double-blind APTIOM study 093-304 found that patients treated with APTIOM as adjunctive therapy for partial-onset seizures had significantly less seizure severity and bother compared to patients in the placebo group as assessed by the Seizure Severity Questionnaire (SSQ).

Methodology and Results
The SSQ is a validated and sensitive multi-dimensional patient-reported assessment to evaluate the severity and bothersomeness of seizures, independent of seizure frequency; lower values indicate improvement. The SSQ was assessed in 441 patients with a valid SSQ total score at baseline and week 14. Among patients treated with APTIOM 800 mg, week 14 LEAST mean square (LSM) values for total score, severity and bothersomeness of ictal movement and altered consciousness during seizures (DS) (ranging from 0 to 1 equal to 50 percent), using the Quality of Life in Epilepsy-31 (QOLE-31) questionnaire. The QOLE-31 is an instrument that assesses daily functioning and overall well-being in patients with epilepsy. The mean change in QOLE-31 Total Score and seven subscale scores (Seizure Worry, Emotional Well-Being, Energy/Fatigue, Cognitive Functioning, Medication Effects, Social Functioning, Overall Quality of Life) from baseline to Week 18 were compared to standard minimal clinically-important difference (MCID) change scores. Results showed the mean change in QOLE-31 Total Score was significantly improved and exceeded the MCID of 5.19 among Completers (mean change was 6.72, p<0.001) and Responders (mean change was 7.71, p<0.001). Significant improvements in all seven subscale scores were observed among Completers (p<0.001) and Responders (p<0.05), and all exceeded the MCID, except for Energy/Fatigue among Responders, and Emotional Well-Being among both Completers and Responders.

Comparing Anti-Epileptic Drug Preferences Between Neurologists and Patients: Results from a National Survey and Discrete Choice Experiment (Poster 5.009, Presented Wednesday, April 20, 2016, 8:30 a.m. This presentation also will be included in the "Practical Approaches to Narrowing the Epilepsy Treatment Gap - Integrated Neuroscience" session on Thursday, April 21, 2016 from 3:00 p.m. to 3:30 p.m. PT as presentation 010.)

A national survey found that people with epilepsy had similar AED preferences to neurologists. The results of this survey also provided additional insights into what AED attributes matter most to people with epilepsy, further reinforcing the importance of the neurologist/patient relationship when making AED treatment decisions.

Methodology and Results
Neurologists and people with epilepsy (≥18 years, treated with AEDs) were recruited from nationally representative U.S. panels to complete an online survey that included a discrete choice experiment component (DCE). Respondents ranked 13 AED attributes by their relative influence on prescribing/treatment decisions (higher value=less influence on AED preference). For the DCE, respondents viewed 15 hypothetical AED sets and selected a preferred AED from each set based on hypothetical profiles related to efficacy, adverse effects (AEs), and convenience. Data from 805 respondents were analyzed (603 patients, 122 general neurologists, 50 epileptologist-neurologists). Results found that patients and neurologists unanimously ranked seizure control; problems with memory, attention, or thought clarity; problems with coordination, balance or falling; problems with feeling fatigued, sleepy or drowsy; and the risk of developing depression, irritability or anxiety as the five most important attributes of AEDs. Patients with incomplete seizure control ranked all attributes significantly higher than the overall patient population (each P<0.05).
and ranked seven of the 13 attributes significantly higher than neurologists (each *P*<0.05). Results from the DCE found that much of the treatment preference for neurologists and patients (63 percent and 49 percent, respectively) was influenced by two variables: seizure control (45 percent of overall influence and 32 percent, respectively) and number of AED pills taken daily (18 percent and 17 percent, respectively). Patients also added the risk of developing psychiatric issues (depression, anxiety, or irritability) as a third important treatment attribute influencing their decision-making (20 percent influence).

**About Aptiom® (eslicarbazepine acetate)**

APTIOM® is the latest member of the dibenzazepine carbamamide family of antiepileptic drugs (AEDs), an established class of medicines. APTIOM® is the only exclusively once-daily, non-extended release AED FDA-approved for use as monotherapy or adjunctive therapy for partial-onset seizures. The precise mechanism(s) by which eslicarbazepine acetate, the primary active metabolite of APTIOM, exerts anticonvulsant activity is unknown but is thought to involve inhibition of voltage-gated sodium channels. APTIOM can be taken whole or crushed, with or without food. APTIOM® is not classified as a controlled substance by the FDA.

The initial research and development of eslicarbazepine acetate was performed by BIAL-Portela & C. S.A. (BIAL), a privately held Portuguese pharmaceutical company. Subsequently, Sunovion acquired the rights under an exclusive license to further develop and commercialize eslicarbazepine acetate in the United States and Canada markets from BIAL. BIAL gained approval for eslicarbazepine acetate from the European Commission on April 21, 2009 as adjunctive therapy in adult patients with partial-onset seizures with or without secondary generalization. In Europe, the product is marketed under the trade name Zebinix®. APTIOM® is approved in Canada for use as adjunctive therapy in the treatment of partial-onset seizures in patients with epilepsy who are not satisfactorily controlled with conventional therapies.

**About Epilepsy and Partial-Onset Seizures**

Epilepsy is the fourth most common neurological condition, and one in 26 people in the U.S. will develop epilepsy in his or her lifetime.1 Epilepsy manifests as unprovoked seizures, which are caused by abnormal firing of impulses from nerve cells in the brain.2 Partial-onset seizures, the most common type of seizure, are characterized by bursts of electrical activity that are initially focused in specific areas of the brain and may become more widespread, with symptoms varying according to the affected areas.2 The unpredictable nature of seizures may have a significant impact on those with epilepsy. Reducing the frequency of seizures may lessen the burden of epilepsy.3 With approximately one-third of people living with epilepsy still unable to control seizures, there continues to be a need for new therapies.4 Up to 40 percent of people living with epilepsy do not respond to the first or second monotherapy5, and approximately 36 percent fail to achieve adequate control of seizures despite the use of two or more antiepileptic medications.6

**Please see important safety information below.**

**Indication:**

Aptiom® (eslicarbazepine acetate) is a prescription medicine used alone or with other medicines to treat partial-onset seizures.

**Important safety information:**

Do not take APTIOM® if you are allergic to eslicarbazepine acetate, any of the other ingredients in APTIOM®, or oxcarbazepine.

**Suicidal behavior and ideation:**

Antiepileptic drugs, including APTIOM® may cause suicidal thoughts or actions in a very small number of people, about 1 in 500. Call your doctor right away if you have any of the following symptoms, especially if they are new, worse or worry you thoughts about suicide or dying: attempting to commit suicide; new or worse depression, anxiety, or irritability; feeling agitated or restless; panic attacks; trouble sleeping (insomnia); acting aggressively; being angry or violent; acting on dangerous impulses; an extreme increase in activity and talking (mania); or other unusual changes in behavior or mood.

**Allergic reactions:**

APTIOM® may cause serious skin rash or other serious allergic reactions that may affect organs or other parts of your body like the liver or blood cells. You may or may not have a rash with these types of reactions. Call your doctor right away if you experience any of the following symptoms: swelling of the face, lips, tongue; trouble swallowing or breathing; hives; fever, swollen glands, or sore throat that do not go away or come and go; painful sores in the mouth or around your eyes; yellowing of the skin or eyes; unusual bruising or bleeding; severe fatigue or weakness; severe muscle pain; or frequent infections or infections that do not go away.

**Low salt (sodium) levels in the blood:**

APTIOM® may cause the level of sodium in your blood to be low. Symptoms may include nausea, tiredness, lack of energy, irritability, confusion, muscle weakness or muscle spasms, or more frequent or more severe seizures. Some medicines can also cause low sodium in your blood. Be sure to tell your health care provider about all the medicines that you are taking.

**Nervous system problems:**

APTIOM® may cause many problems that can affect your nervous system, including dizziness, sleepiness, vision problems, trouble concentrating, and difficulties with coordination and balance. APTIOM® may slow your thinking or motor skills. Do not drive or operate heavy machinery until you know how APTIOM affects you.

**Liver problems:**

APTIOM® may cause problems that can affect your liver. Symptoms of liver problems include yellowing of your skin or the whites of your eyes, nausea or vomiting, loss of appetite, stomach pain, or dark urine.

**Most common adverse reactions:**

The most common side effects in patients taking APTIOM® include dizziness, sleepiness, nausea, headache, double vision, vomiting, feeling tired, problems with coordination, blurred vision, and Shakiness.

**Drug interactions:**

Tell your health care provider about all the medicines you take, including prescription and over-the counter medicines, vitamins, and herbal supplements. Taking APTIOM® with certain other medicines may cause side effects or affect how well they work. Do not start or stop other medicines without talking to your health care provider. Especially tell your health care provider if you take oxcarbazepine, carbamazepine, phenobarbital, phenytoin, primidone, clobazam, oneprazole, imatinib, or rosvastatin, or birth control medicine.

**Discontinuation:**

Do not stop taking APTIOM® without first talking to your health care provider. Stopping APTIOM® suddenly can cause serious problems.

**Pregnancy and lactation:**

APTIOM® may cause your birth control medicine to be less effective. Talk to your health care provider about the best birth control method to use. APTIOM® may harm your unborn baby. APTIOM® passes into breast milk. Tell your health care provider if you are pregnant or plan to become pregnant, or are breast-feeding or plan to breastfeed. You and your health care provider will decide if you should stop taking APTIOM®. If you become pregnant while taking APTIOM®, talk to your health care provider about registering with the North American Antiepileptic Drug (NAAED) Pregnancy Registry. The purpose of this registry is to collect information about the safety of antiepileptic medicine during pregnancy. You can enroll in this registry by calling 1-888-233-2334.

**Get medical help right away if you have any of the symptoms listed above.** You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch or call 1-800-FDA-1088.

For more information, please see the APTIOM® Medication Guide[3] and Full Prescribing Information[4].

**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 spirit of innovation is driven by the conviction that scientific excellence paired with meaningful advocacy and relevant education can improve lives. The Company 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. Sunovion’s track record of discovery, development and commercialization of important therapies has included Brovana® (afornomotortol tartrate), Latuda® (lurasidone HCI), and most recently Aptiom® (eslicarbazepine acetate).


Additional information can be found on the Company’s web sites: www.sunovion.com[5], www.sunovion.eu[6] and www.sunovion.ca[7]. Connect with Sunovion on Twitter @Sunovion[8] and LinkedIn[9].

**About Sumitomo Dainippon Pharma Co., Ltd.**

Sumitomo Dainippon Pharma is a top-ten listed pharmaceutical company in Japan. Sumitomo Dainippon Pharma aims to produce innovative pharmaceutical products in the Psychiatry & Neurology area and the Oncology area, 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 about 7,000 employees worldwide. Additional information about Sumitomo Dainippon Pharma is available through its corporate website at www.ds-pharma.com[11].

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References


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