News Release

Contact: Jennifer Baird
Director, Corporate Communications
Sunovion Pharmaceuticals Inc.
(508) 787-4109
jennifer.baird@sunovion.com

Sunovion Announces Results of Health Outcomes Analyses Exploring the Effectiveness of Aptiom® (eslicarbazepine acetate) in People with Partial-Onset Seizures

Marlborough, Mass., December 6, 2015 – Sunovion Pharmaceuticals Inc. (Sunovion) announced results of Health Economics and Outcomes Research (HEOR) analyses from two Phase 3 Aptiom® (eslicarbazepine acetate) monotherapy clinical trials; and a claims analysis of a large database of patients with epilepsy. The results were presented during the 69th American Epilepsy Society (AES) Annual Meeting in Philadelphia.

In August 2015, Sunovion announced that the U.S. Food and Drug Administration (FDA) approved the use of APTIOM as monotherapy for the treatment of partial-onset seizures. APTIOM may be used as monotherapy in people who initiate treatment for the first time or convert from other antiepileptic drugs (AEDs) to APTIOM.

A post-hoc pooled analysis of two historical-controlled Phase 3 APTIOM monotherapy clinical trials (Studies 093-045 and 093-046) showed that patients with partial-onset seizures who achieved a clinical response after converting from a multi-AED regimen to APTIOM monotherapy experienced quality of life improvements after 10 weeks. A separate analysis of these studies also showed that patients with partial-onset seizures experienced statistically and clinically significant improvements in depressive symptoms after 10 weeks, following successful conversion from their current AED regimen to APTIOM monotherapy.

During AES, Sunovion also presented an analysis from the IMS PharMetrics Plus database. The results indicated that, after controlling for baseline confounders, patients initiating AED therapy with one pill/day had fewer annual hospitalizations and emergency room visits than initiating AED therapy with two or more pills/day.

“Seizures account for one million emergency department visits every year, and epilepsy has significant impacts on a person's ability to drive or maintain employment,” said Krithika Rajagopalan, Head of Global Health Economics and Outcomes Research, Sunovion. “Quality of life assessments provide insights into measurable factors that are important in determining potential treatment outcomes. These results suggest
improved seizure control with AED monotherapy is correlated with overall improvements in specific aspects of daily life, as well as fewer hospitalizations. Sunovion is committed to providing health outcomes data that may contribute to improved treatment approaches for people living with partial-onset seizures.”

Summary of Highlighted HEOR Poster Presentations

**Quality of Life Improvement among Patients with Refractory Partial-Onset Seizures: A Clinical Trial Analysis of Patients who Responded to Eslicarbazepine Acetate Monotherapy (Poster 1.182, Presented Saturday, December 5, 2015, 12:00 p.m. – 6:00 p.m. ET)**

Pooled data from two historical-controlled Phase 3 studies (093-045 and 093-046) evaluated patients who had completed 10 weeks of APTIOM monotherapy (n=224) for change in health-related quality of life, using Quality of Life in Epilepsy-31 (QOLIE-31) questionnaire. The QOLIE-31 is an instrument that assesses daily functioning and overall well-being in patients with epilepsy. The mean change in QOLIE-31 Total Score and seven subscale scores from baseline to Week 18 were compared to standard minimal clinically-important difference (MCID) change scores. The results showed that the mean change in QOLIE-31 Total Score and five of the seven subscales (Medication Effects, Seizure Worry, Social Functioning, Overall Quality of Life, Cognitive Functioning, and Energy/Fatigue) were greater than their respective MCIDs; these changes were statistically significant for Medication Effects (p=0.011), and Social Functioning (p=0.008).

**Change in Depressive Symptoms Among Patients With Refractory Partial-Onset Seizures Treated With Eslicarbazepine Acetate Monotherapy: A Pooled Analysis of Clinical Trials (Poster 2.249, Presented Sunday, December 6, 8:00 a.m. – 4:00 p.m. ET)**

Pooled data from two historical-controlled Phase 3 studies (093-045 and 093-046) evaluated patients who had completed 10 weeks of APTIOM monotherapy (Completers, n=224), as well as a subset of these patients who achieved a clinical response after 10 weeks of treatment (Responders, n=117), for change in depressive symptoms, using the Montgomery-Åsberg Depression Rating Scale (MADRS) questionnaire. The MADRS is a 10-item instrument used to identify moderate-to-severe depressive symptoms. MADRS scores were compared to 1) Population-level MCID change scores (range: 1.3 to 1.6); and 2) Treatment effect MCID change scores (1 point versus active treatment or 2 points versus placebo).

Data showed that mean change in the MADRS scores was significantly decreased (indicating a reduction in depressive symptoms) and exceeded published MCID change scores (-2.1 for Completers and -2.6 for Responders, p<0.001 for both). Over half of all patients in these groups (56.3 percent of Completers and 56.4 percent of Responders) experienced significant reductions in depressive symptoms—with most patients (90.5 percent and 87.9 percent, respectively) reporting decreased MADRS scores of two or more points.
The Association Between Antiepileptic Drug Pill Burden at Monotherapy Initiation and Epilepsy-Related Hospital Admissions and Emergency Department Visits in the US (Poster 2.282, Presented Sunday, December 6, 8:00 a.m. – 4:00 p.m. ET)

A retrospective analysis of health insurance claims data from more than 53,000 epilepsy patients who initiated AED monotherapy found that patients who initiated with a one pill/day regimen had fewer hospitalizations and emergency room visits over the following 12 months compared with patients initiating with two or more AEDs. Patients initiating with two, three, or more than three pill/day regimens had annual hospitalization rates that were 12.5, 23.1, and 19.4 percent higher respectively, compared to patients taking one pill/day. Patients initiating with larger pill burdens also had significantly higher rates of emergency room visits during the year of follow-up (15.5, 25.2, and 15.1 percent higher for patients taking two, three, or more than three pills/day, respectively).

About the Phase 3 Monotherapy Studies
Two identically designed Phase 3, dose-blinded, historical-controlled, multi-center, randomized clinical trials (Studies 093-045 and 093-046) evaluated the safety and efficacy of APTIOM (1,600 mg/day or 1,200 mg/day) as monotherapy for partial-onset seizures in patients 16 years of age or older whose seizures were not well-controlled with other antiepileptic drugs (AEDs).

The primary endpoint for both trials was the percentage of patients who exited the study due to pre-defined criteria identifying worsening seizure control, compared to historical controls from previous, similarly designed trials of epilepsy patients converting to AED monotherapy. Trial results showed that conversion to APTIOM monotherapy was associated with exit rates superior to historical controls in patients with partial-onset seizures, who were not well-controlled by one or two current AEDs.

APTIOM administered once-daily was generally well tolerated in both dose strengths. In the APTIOM monotherapy trials, the most common treatment-related adverse events, headache, dizziness, fatigue, somnolence, and nausea, were mainly mild or moderate in severity.

About Aptiom® (eslicarbazepine acetate)
APTIOM is the latest member of the dibenzazepine carboxamide family of antiepileptic drugs (AEDs), an established class of medicines. APTIOM is the only exclusively once-daily, non-extended release AED now FDA-approved for use as monotherapy or adjunctive therapy for partial-onset seizures. The precise mechanism(s) by which eslicarbazepine, 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 & Ca, S.A. (BIAL), a privately held Portuguese research-based 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 Medicines Agency 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 therapy.

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.³ 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.⁴ With approximately one-third of people living with epilepsy still unable to control seizures, there continues to be a need for new therapies.⁵ Up to 40 percent of people living with epilepsy do not respond to the first or second monotherapy⁶, and approximately 36 percent fail to achieve adequate control of seizures despite the use of two or more antiepileptic medications⁷.

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: APTIOM may cause suicidal thoughts or actions, depression, or mood problems. Call your doctor right away if you experience these or any other effects or reactions: 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 aggressive; 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, eyes, lips, or 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 healthcare provider about all the other medicines that you are taking.

**Nervous system problems:** APTIOM may cause 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 healthcare 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 healthcare provider.** Especially tell your healthcare provider if you take oxcarbazepine, carbamazepine, phenobarbital, phenytoin, primidone, clobazam, omeprazole, simvastatin, rosuvastatin, or birth control medicine.

**Discontinuation:** Do not stop taking APTIOM without first talking to your healthcare 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 healthcare provider about the best birth control method to use. APTIOM may harm your unborn baby. APTIOM passes into breast milk. Tell your healthcare provider if you are pregnant or plan to become pregnant, or are breastfeeding or plan to breastfeed. You and your healthcare provider will decide if you should take APTIOM. If you become pregnant while taking APTIOM, talk to your healthcare 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](http://www.fda.gov/medwatch) or call 1-800-FDA-1088.

For more information, please see the [APTIOM Medication Guide](#) and [Full Prescribing Information](#).

**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® (arformoterol tartrate), Latuda® (lurasidone HCl), and most recently Aptom® (eslicarbazepine acetate).

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 web sites: [www.sunovion.com](http://www.sunovion.com), [www.sunovion.eu](http://www.sunovion.eu) and [www.sunovion.ca](http://www.sunovion.ca). Connect with Sunovion on Twitter [@Sunovion](https://twitter.com/Sunovion) and [LinkedIn](https://www.linkedin.com/company/sunovion).

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References


