

New data reinforce the efficacy and safety profile of Sativex® in Multiple Sclerosis Spasticity

- **Results of a new long-term, placebo-controlled trial support sustained efficacy of Sativex (THC:CBD oromucosal spray) without cognition or mood impairment**
- **New study data also shows that Sativex does not cause impairment of motor vehicle driving ability**
- **Sativex's real world tolerability has now been demonstrated from registries in Germany, Spain and UK with >800 patients**

Copenhagen, Denmark, 2nd October 2013: Almirall S.A. (ALM) today announces the latest evidence with Sativex® (THC:CBD spray) from new MS spasticity studies (clinical trial data, observational study data and registries data collection). These data, presented today at the 29th Congress of the European Committee for Treatment and Research in Multiple Sclerosis (ECTRIMS) in Copenhagen, Denmark, show that Sativex® effectiveness is maintained long term with no additional safety concerns identified in clinical practice.

Two-thirds of the more than 2,000 patients with MS surveyed in the recent Spanish "6E" study reported a certain degree of spasticity, being moderate or severe in 40% of themⁱ.

"Sativex can improve the spasticity symptoms impairment of MS patients without affecting such issues as driving ability, cognition or mood", says Dr. Tiina Rekand, of the Haukeland University Hospital Bergen, Norway.

Most patients with MS experience a degree of spasticity which is associated with increasing disability and therefore rising healthcare costs. Spasticity has a negative impact on those patients' quality of life as it reduces their capacity to carry out everyday activities, as well as having an impact on the already impaired general mobility, bladder function, fatigue and quality of sleep.

"Sativex® provides symptomatic treatment of MS spasticity in patients who have not responded to other medicines. It has proven to reduce significantly patients' rigidity and spasms frequency leading to an improved sleep quality and better performing of daily activities. This means greater independence for patients, requiring less help from family members or carers", add Dr. Carlo Pozzilli, of the Multiple Sclerosis Centre Sant' Andrea Hospital, Rome, Italy.

Improving MS spasticity symptoms without affecting patient's abilities

The lack of effects on patient cognition and mood from Sativex are some of the new data presented at the ECTRIMS 2013 congress. A double-blind, randomised, placebo-controlled Phase IV study was carried out in MS specialised EU centres. After 50 weeks of treatment with Sativex spray, (mean dose 6.4 sprays/day) findings

demonstrated equivalence to placebo stable status both in cognition and mood scales. The improvements in spasticity were confirmed by more than 70% of patients (Global impression of change (GIC)), but also by physicians and carers, always significantly different to the placebo treated group. Treatment with Sativex® was generally well tolerated.

Another new study, which was prospective and observational, conducted in three German centres during the first four to six Sativex treatment weeks (mean dose 5.2 sprays/day), showed no adverse effects on driving ability (no significant changes vs. baseline in a battery of computerized tests)). The MS spasticity and spasms count improved and the treatment was again well tolerated.

Sativex UK, Germany and Spain registries have recruited approximately 700 patients to date without signals of new tolerability/safety concerns (falls, addiction, etc.) and over 20,000 patient/years of use are estimated without any relevant pharmacovigilance issues.

Recent guidelines, such as the German DGN 2012, recommend a role for THC:CBD spray in the management of MS spasticity.

Prof. Koehler presented his large German centre experience with Sativex® in everyday clinical practice.

“Sativex has become a useful tool for relieving the problems of resistant to previous medication MS spasticity patients, acting on relevant quality of life impairments or marked associated symptoms such as pain, sleep disruptions or bladder dysfunction”, says Prof. Koehler's, of the Marianne Strauss Clinic, Berg, Germany.

In Europe, Sativex® is commercialized for the treatment of MS spasticity in the UK, Spain, Germany, Denmark, Norway, Italy, Poland and Sweden. Launches are also currently in preparation in Switzerland, Austria, Iceland, Finland and others countries. In addition, regulatory authorization has been received in Belgium, Finland, the Netherlands, Portugal, Czech Republic and Slovakia with launches expected from the end of 2013 onwards.

In addition to MS spasticity, Sativex®, is also being developed by GW Pharmaceuticals, for the treatment of cancer pain. Almirall holds the marketing rights to this medicine in Europe (except the United Kingdom) and Mexico.

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Notes to Editors

About Sativex®

Sativex® is an endocannabinoid system modulator made of two active principles - THC (delta-9-tetrahydrocannabinol) and CBD (cannabidiol)-, which was developed and its manufactured by GW Pharmaceuticals plc, UK. Almirall holds marketing rights in Europe (except United Kingdom) and Mexico.

Sativex[®] is indicated as a treatment for adult patients with moderate to severe spasticity due to multiple sclerosis (MS) who have not adequately responded to other anti-spasticity medications and who have demonstrated a clinically significant improvement in symptoms related to spasticity during an initial treatment testing periodⁱⁱ. Sativex[®] is effective in all types of MS, independently of the disability status (as per Expanded Disability Status Scale –EDSS) a rating system that is frequently used for classifying and standardizing the condition of people with multiple sclerosis).ⁱⁱⁱ

Sativex[®] contains active ingredients known as ‘cannabinoids’, which are extracted from the plant *C. Sativa* grown and processed under strictly controlled conditions. Cannabinoids react with cannabinoid receptors that exist naturally throughout our body, including the brain.^{iv} A receptor is a site located in a brain cell in which certain substances can stick or “bind” for a while. If this happens, this binding has an effect on the cell and the nerve impulses it produces, causing a ‘dimming-down’ of the spasticity symptom. In patients who respond to Sativex[®], this is the effect that improves their spasticity symptoms and helps them cope with their daily activities.^v

In addition to MS spasticity, Sativex[®], which has been developed by GW Pharmaceuticals, is also in phase III clinical development for the treatment of cancer pain.

Spasticity

In the five main EU markets there are around 500,000 people suffering from MS^{vi}. Spasticity is a symptom defined by patients and carers as muscle spasms, stiffness and/or difficulty in moving muscles and it is one of the most common symptoms of MS, occurring in up to 75% of MS sufferers in the course of the disease. Spasticity can affect many aspects of the daily lives of patients with MS and is one of the main factors contributing to their distress and disability.^{vii}

Almirall

Almirall is a pharmaceutical company committed to providing valuable medicines through our own R&D efforts, which exceeded 23 per cent of sales in 2012, together with external partnerships, licenses and collaborations. We seek to provide innovative medicines to treat respiratory and dermatology diseases, with a strong interest in gastroenterology and pain.

With more than 3000 employees in 22 countries, Almirall generated total revenues that exceeded 1 billion dollars in 2012.

The company was founded in 1943 and is headquartered in Barcelona, Spain. The stock is traded on the Spanish stock exchange (ticker: ALM).

For more information please visit: www.almirall.com

ⁱ C. Oreja-Guevara, D. González-Segura, and C. Vila. Spasticity in multiple sclerosis: results of a patient survey. *Int J Neurosci*, 2013; Early Online: 1–9

ⁱⁱ Patient leaflet

ⁱⁱⁱ *A randomized, double-blind, placebo-controlled, parallel-group, enriched-design study of nabiximols (Sativex[®]), as add-on therapy, in subjects with refractory spasticity caused by multiple sclerosis* - Novotna A. et al, *European Journal of Neurology* 2011 – Sept ; 18(9):1122-31.

^{iv} GW Pharmaceuticals: Cannabinoid Science: Mechanism of action. Available at: <http://www.gwpharm.com/mechanism-of-action.aspx> (latest access: 26/04/2012).

^v GW Pharmaceuticals: Cannabinoid Science: Cannabinoid Compounds. Available at <http://www.gwpharm.com/types-compounds.aspx> (Last accessed: 26/04/12).

^{vi} Multiple Sclerosis International Federation: European map of ms database. ©2010 EMSP, MSIF. Available at: www.europeanmapofms.org (latest access: 11/08/2010). *Top five EU countries include: France, Germany, Italy, Spain and UK.*

^{vii} Rizzo MA *et al.* Prevalence and treatment of spasticity reported by multiple sclerosis patients. *Mult Scler* 2004;10:589–595.