

## Positive data in sativex® phase IIb trial: Support advancing into phase III development in cancer pain

**Datos positivos en el ensayo de fase IIb con sativex(R). Apoyo para el avance al desarrollo de la fase III en el dolor del cáncer**

*Dear Editor*

Porton Down, UK; 23 March 2010: GW Pharmaceuticals plc (AIM: GWP) today announced preliminary results of a Phase IIb dose-ranging trial evaluating the efficacy and safety of Sativex® in the treatment of pain in patients with advanced cancer, who experience inadequate analgesia during optimized chronic opioid therapy. This trial was performed in conjunction with GW's licensing partner for Sativex in the United States—Otsuka Pharmaceutical Co. Ltd.

In Europe, Sativex is in the advanced stages of a regulatory submission in the UK and Spain as a treatment for multiple sclerosis spasticity with approvals expected in Q2 2010. In the US, cancer pain represents the initial target indication for Sativex.

Key points:

- study meets key objectives of providing data to support entry into Phase III,
- Sativex shows statistically significant differences from placebo in pain scores, according to both continuous response analysis and change from baseline analysis in NRS average pain,
- GW and Otsuka now planning End of Phase II meeting with the FDA to gain endorsement of the proposed Phase III program.

Dr. Stephen Wright, GW's R&D Director, said, "We are very pleased to have successfully completed two Phase II studies showing positive data supporting the efficacy of Sativex in cancer pain. We are now working closely with Otsuka in preparing for Phase III development of Sativex in the United States market."

Commenting on the results, the principal investigator, Dr. Russell K. Portenoy, Chairman of the Department of Pain Medicine and Palliative Care at Beth Israel Medical Center in New York City, said, "Many patients with advanced cancer do not attain adequate pain relief from an opioid regimen, or experience opioid side effects that call for strategies that may be able to lower the opioid requirement while providing equivalent or better analgesia. A key strategy involves the administration of a co-analgesic drug. The encouraging data from this study provide a strong rationale for developing a cannabinoid for this purpose. I look forward to the Phase III development of Sativex."

## Study results

The primary objectives of this study were to generate sufficient efficacy and safety information to justify

continuing into Phase III development, to determine the effective dose range of Sativex in this patient population, and to determine the optimal study parameters to be used in Phase III studies.

Preliminary results show that the study met its key objectives and provided efficacy and safety data that support advancing to Phase III clinical trials.

This randomized double-blind placebo-controlled parallel-group study recruited a total of 360 patients in 14 countries in North America, Europe, Latin America, and South Africa, and evaluated three dose ranges of Sativex—a low dose (1–4 sprays per day), mid dose (6–10 sprays per day), and high dose (11–16 sprays per day) over a 5 week treatment period. Patients received active or placebo as add-on treatment to strong opioid therapy and remained on stable doses of their background optimized opioid therapy during the study.

The primary efficacy measure of the study was a patient assessment of pain using a 0–10 numeric rating scale (NRS) that was analyzed using three conventional methodologies, including 30% responder analysis, continuous response analysis as well as change from baseline analysis in NRS average pain. Two of the three analyses showed statistically significant results in favor of Sativex.

The 30% responder analysis, which was the primary analysis specified in the protocol, was numerically in favor of Sativex but did not show a statistical difference compared to placebo. The "continuous response analysis" (an analysis of all response levels characterized by percent improvement), did show statistically significant results in favor of Sativex for both Sativex low and mid dose groups vs. placebo ( $p=0.008$  and  $p=0.038$ , respectively). The low and mid dose Sativex groups, when combined, were also significantly superior to placebo ( $p=0.006$ ). In the United States, this continuous response analysis has been the key efficacy parameter discussed in the product labeling of several recently approved medicines for pain.

The change from baseline in NRS average pain score showed a statistically significant difference between the Sativex low dose group and placebo ( $p=0.006$ ). The low and mid dose Sativex groups, when combined, were also statistically significantly superior to placebo ( $p=0.019$ ).

For the notable secondary endpoint of sleep disruption, the Sativex low dose group also showed a statistically significant difference vs. placebo in reducing sleep disruption ( $p=0.003$ ). The low and mid dose Sativex groups, when combined, also showed a statistically significant reduction in sleep disruption compared with placebo ( $p=0.016$ ).

The Sativex high dose level was less well tolerated than the low and mid dose groups. Discontinuation due to adverse events was 22% in the high dose group, and was substantially higher than the rates of discontinuation in the placebo (10%), low dose (5%), and middle dose (7%) groups. In addition, the high dose group did not show a profile of efficacy that was better than the placebo group in this study.

The safety profile of Sativex in this Phase IIb study is consistent with previous studies in this patient population. The most common adverse events (> 10% for the combined Sativex population) reported for the Sativex treatment groups were nausea (22% vs. 13% for placebo), dizziness (19% vs. 13% for placebo), neoplasm progression (18% vs. 14% for placebo), vomiting (16% vs. 8% for placebo), and somnolence

(15% vs. 4% for placebo). The adverse event profile for the Sativex low dose group compared favorably to placebo.

The results of this Phase IIb dose ranging study are consistent with a previous Phase IIa, 3-week clinical trial in 177 patients conducted by GW. In this prior study, Sativex showed a statistically significant improvement vs. placebo in the continuous response analysis ( $p=0.044$ ), as well as the mean change from baseline in NRS pain score ( $p=0.014$ ). This study was recently published in the *Journal of Pain and Symptom Management*.<sup>1</sup>

This study is the first major trial carried out by GW and Otsuka as part of the development program aimed at securing regulatory approval for Sativex from the FDA.

As previously planned, GW and Otsuka anticipate holding an End of Phase II Meeting with the FDA within the next few months prior to commencing the Phase III program. The current US development program anticipates two further Phase III trials prior to a subsequent submission of a new drug application to the FDA.

There will be a conference call for analysts today at 8.30am. Analysts should contact Juliet Edwards at Financial Dynamics on +4420 7269 7125 for details.

A recording of this call will be available later today on the presentations/webcasts page in the investor relations section of the GW website ([www.gwpharm.com](http://www.gwpharm.com)).

## Notes to Editors

### Sativex

Sativex is an investigational new product composed primarily of two cannabinoids: CBD (cannabidiol) and THC (delta 9 tetrahydrocannabinol). Sativex is administered as a metered dose oro-mucosal spray; each 100 µL spray contains 2.7 mg THC and 2.5 mg CBD. The Sativex formulation is standardized by both composition and dose and is supplied in small spray vials. The components of Sativex have been shown to bind to cannabinoid receptors that are distributed throughout the central nervous system and in immune cells.

Cancer pain represents the initial target indication for Sativex in the US. Outside the US, Sativex is in the advanced stages of a regulatory submission in the UK and Spain as a treatment for multiple sclerosis spasticity. Approval in the UK and Spain is expected in Q2 2010. Sativex is also approved in Canada for indications of cancer pain and multiple sclerosis neuropathic pain under Health Canada's Notice of Compliance with conditions (NOC/c) policy.

### Cancer pain

Studies suggest that more than one third of patients with cancer, and more than three quarters of those with advanced disease, have chronic pain. Large surveys indicate that optimal opioid therapy does not yield sufficient relief in a substantial proportion of these patients.

### About GW–Otsuka

In February 2007, GW and Otsuka entered into a major long term strategic alliance. The relationship commenced with

the signing of an exclusive license agreement to develop and market Sativex<sup>®</sup>, GW's lead product, in the US. In July 2007, GW and Otsuka signed a global research collaboration for the study of cannabinoids in the field of central nervous system (CNS) and oncology to research, develop, and commercialize a range of candidate cannabinoid products.

### About Otsuka Pharmaceutical Co., Ltd.

Founded in 1964, Otsuka Pharmaceutical Co., Ltd. is a global healthcare company with the corporate philosophy: "Otsuka-people creating new products for better health worldwide." Otsuka researches, develops, manufactures, and markets innovative and original products, with a focus on pharmaceutical products for the treatment of diseases and consumer products for the maintenance of everyday health. Otsuka is committed to being a corporation that creates global value, adhering to the high ethical standards required of a company involved in human health and life, maintaining a dynamic corporate culture, and working in harmony with local communities and the natural environment. Otsuka Pharmaceutical Co., Ltd. is a wholly owned subsidiary of Otsuka Holdings Co., Ltd., the holding company for the Otsuka Group. The Otsuka Group comprises 153 companies and employs approximately 36,000 people in 23 countries and regions worldwide. Otsuka and its consolidated subsidiaries earned ¥955.9 billion (approximately US \$9.7 billion<sup>c</sup>) in annual revenues in fiscal 2008.

### About GW

GW was founded in 1998 and listed on AiM, a market of the London Stock Exchange, in June 2001. Operating under license from the UK Home Office, the company researches and develops cannabinoid pharmaceutical products for patients who suffer from a range of serious ailments, in particular multiple sclerosis and cancer pain. GW has assembled a large in-house scientific team with expertise in cannabinoid science as well as experience in the development of both plant-based prescription pharmaceutical products and medicines containing controlled substances. GW occupies a world leading position in cannabinoids and has developed an extensive international network of the most prominent scientists in the field. For further information, please visit [www.gwpharm.com](http://www.gwpharm.com).

This news release may contain forward-looking statements that reflect GW's current expectations regarding future events, including development and regulatory clearance of the GW's products. Forward-looking statements involve risks and uncertainties. Actual events could differ materially from those projected herein and depend on a number of factors, including (inter alia) the success of the GW's research strategies, the applicability of the discoveries made therein, the successful and timely completion of uncertainties related to the regulatory process, and the acceptance of Sativex<sup>®</sup> and other products by consumer and medical professionals.

<sup>c</sup>Exchange rate as of March 31, 2009.

## Reference

1. Johnson J. Journal of Pain and Symptom Management 2000;39:167–9.

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