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## **GW Pharmaceuticals and Otsuka Announce Results From Two Remaining Sativex(R) Phase 3 Cancer Pain Trials**

- Consistent with previously announced results from the initial Phase 3 trial, remaining trials fail to show superiority over placebo
- Pre-specified subgroup analyses of pooled U.S. patients demonstrated a statistically significant result for the primary endpoint and a number of secondary endpoints -
- GW and Otsuka have submitted a request to meet with FDA to discuss clinical relevance of U.S. data and potential paths forward -

LONDON and PRINCETON, N.J., Oct. 27, 2015 (GLOBE NEWSWIRE) -- GW Pharmaceuticals plc (NASDAQ:GWPH) (AIM:GWP) ("GW") and Otsuka Pharmaceutical Development & Commercialization, Inc. ("Otsuka"), today reported top-line results from the remaining two Phase 3 trials for the investigational product Sativex® in the treatment of pain in patients with advanced cancer who experience inadequate analgesia during optimized chronic opioid therapy. Consistent with the previously reported Phase 3 trial, Sativex did not meet the primary endpoint in these trials. However, a pre-specified pooled analysis of patients across the two Phase 3 trials which involved clinical sites in the U.S. showed a statistically significant improvement for Sativex compared with placebo ( $p=0.024$ ), with several secondary efficacy endpoints exhibiting  $p$ -values of less than 0.05. GW and Otsuka have submitted a request to meet with the U.S. Food and Drug Administration (FDA) to discuss the clinical relevance of these data and to determine potential paths forward.

"In light of the missed primary endpoint in the first trial earlier this year, these additional results are not a surprise. Nevertheless, we are encouraged by data across the trials which consistently show positive outcomes for U.S. patients when analysed as a separate cohort," stated Justin Gover, GW's Chief Executive Officer. "We believe that this finding may provide important guidance in determining the optimal target patient population for Sativex and look forward to a discussion with the FDA on a potential path forward."

"While the results overall have been disappointing, and not necessarily wholly consistent with clinical experience, nonetheless they suggest that Sativex may have a useful role in the treatment of certain subgroups of patients with advanced cancer pain who have exhausted opioid treatments," stated Dr. Marie Fallon, Professor of Palliative Care, University of Edinburgh and a principal investigator in the Phase 3 program. "In particular, the U.S. patients enrolled in this program showed a useful therapeutic benefit whereas results in European patients were generally not favorable. These U.S. patients were less frail, hence the Sativex intervention was subjected to less "noise," providing clearer results and valuable guidance in determining the optimal target patient population for Sativex. This is a patient population with a significant unmet need and I believe that this important observation for Sativex warrants further investigation."

### **Trial 2 Efficacy**

This randomized, double-blind, placebo-controlled, parallel-group study was identical in design to the previously reported Phase 3 trial. The trial recruited a total of 397 patients at clinical sites in the U.S., Mexico and Europe. Patients received Sativex or placebo as adjunctive treatment to optimized opioid therapy and remained on stable doses of their background opioid therapy during the study.

The primary efficacy measure of this study was a patient assessment of pain using a 0-to-10 Numeric Rating Scale (NRS) which was analysed using percent improvement from baseline as the primary analysis. In addition, improvement was also analysed using a cumulative-proportion-of-responders analysis, which analyses the full range of responses achieved across the entire patient population within a trial.

In this trial, the primary endpoint was in favour of Sativex and approached statistical significance for the intention-to-treat (ITT) population ( $p=0.085$ ). The secondary endpoints followed the pattern of the primary endpoint with a significant reduction seen in sleep disruption ( $p=0.027$ ) and a number of other endpoints approaching statistical significance.

### **U.S. Analyses**

In this study, the U.S. was the largest single recruiting country, with patients from the U.S. representing 30 percent of the overall trial population. The efficacy data from U.S. sites alone showed more positive trends than those in non-U.S. sites, which is consistent with data from the first Phase 3 trial and the Phase 2b trial.

In pre-specified pooled analyses of both this trial and the previously reported Phase 3 trial, which had an identical design, patients at clinical sites in the U.S. (n=248) demonstrated a statistically significant result for the primary endpoint (p=0.024) as well as a number of secondary endpoints including subject global impression of change (p=0.0004) and physician global impression of change (p < 0.0001).

### **Trial 3 Efficacy**

A third study, which was conducted entirely outside the U.S. and which used a different clinical design, failed to show separation from placebo on the primary endpoint.

### **Safety**

The safety profile of Sativex in the clinical development program in treatment of pain in patients with advanced cancer who experience inadequate analgesia during optimized chronic opioid therapy was consistent with the known effects of Sativex and with the clinical profile of this specific patient population. The only adverse event (apart from progression of the underlying cancer) reported at greater than 10 percent for the Sativex population was nausea (15.6% Sativex vs 10.6% placebo in Trial 2).

All three Sativex Phase 3 studies were carried out by GW and Otsuka as part of the development program aimed at securing regulatory approval for Sativex in cancer pain.

### **About Otsuka**

Otsuka Pharmaceutical Development & Commercialization, Inc. (OPDC) is an innovative, fast-growing healthcare company that discovers and develops new compounds that address unanswered medical needs and advance human health. With a strong focus on neuroscience, oncology, and cardio-renal treatments, OPDC is dedicated to improving the health and quality of human life. For more information, visit [www.otsuka-us.com](http://www.otsuka-us.com).

OPDC is a subsidiary of Otsuka America, Inc. (OAI), a holding company established in the U.S. in 1989. OAI is wholly owned by Otsuka Pharmaceutical Co., Ltd. The Otsuka Group employs approximately 43,000 people globally and its products are available in more than 80 countries worldwide. Otsuka welcomes you to visit its global website at <https://www.otsuka.co.jp/en/>.

### **About GW Pharmaceuticals**

*GW is a biopharmaceutical company focused on discovering, developing and commercializing novel therapeutics from its proprietary cannabinoid product platform in a broad range of disease areas. In 17 years of operations, GW has established a world leading position in the development of plant-derived cannabinoid therapeutics through its proven drug discovery and development processes, intellectual property portfolio and regulatory and manufacturing expertise. GW commercialized the world's first plant-derived cannabinoid prescription drug, Sativex<sup>®</sup>, which is approved for the treatment of spasticity due to multiple sclerosis in 27 countries outside the United States. GW is advancing an orphan drug program in the field of childhood epilepsy with a focus on Epidiolex<sup>®</sup>, which is in Phase 3 clinical development for the treatment of Dravet syndrome and Lennox-Gastaut syndrome, two rare and extremely debilitating epilepsy syndromes that begin in infancy or early childhood. Epidiolex is also expected to enter Phase 3 clinical trials in the treatment of Tuberous Sclerosis Complex. GW has a deep pipeline of additional cannabinoid product candidates which includes compounds in Phase 1 and 2 development for both orphan (Neonatal Hypoxic Ischemic Encephalopathy and glioma) and non-orphan (type 2 diabetes and schizophrenia) indications. For further information, please visit [www.gwpharm.com](http://www.gwpharm.com).*

### **Forward-looking statements**

*This news release contains forward-looking statements that reflect GW's current expectations regarding future events, including statements regarding financial performance, the timing of clinical trials, the relevance of GW products commercially available and in development, the clinical benefits of Sativex<sup>®</sup> and the safety profile and commercial potential of Sativex. 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 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, Epidiolex and other products by consumer and medical professionals. A further list and description of risks and uncertainties associated with an investment in GW can be found in GW's filings with the U.S. Securities and Exchange Commission. Existing and prospective investors are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date hereof. GW undertakes no obligation to update or revise the information contained in this press release, whether as a result of new information, future events or circumstances or otherwise.*

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