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Acacia Pharma Group plc: BAREMSIS® PREVENTS POST-OPERATIVE NAUSEA & VOMITING IN HIGH-RISK PATIENTS

ACACIA PHARMA'S BAREMSIS® PREVENTS POST-OPERATIVE NAUSEA & VOMITING IN HIGH-RISK PATIENTS

Positive Phase 3 Clinical Trial Published in Peer-reviewed Journal, *Anesthesiology*

Cambridge, UK and Indianapolis, US - 15 March 2018: Acacia Pharma Group plc ("Acacia Pharma", the "Company" or the "Group"), (EURONEXT: ACPH), a hospital pharmaceutical company focused on the development and commercialisation of new nausea & vomiting treatments for surgical and cancer patients, announces that data and analysis from its Phase 3 prophylaxis trial with intravenous amisulpride (BAREMSIS®) in combination with standard antiemetics have been published in the Online First edition of *Anesthesiology*, the peer-reviewed medical journal of the American Society of Anesthesiologists (ASA) ([Kranke et al.](#)). Positive headline results were first announced by the Company in January 2016.

The Phase 3 trial demonstrated that BAREMSIS is safe and resulted in a statistically significant reduction in the emergence of post-operative nausea & vomiting (PONV) when given in combination with an antiemetic drug from another class to adult patients undergoing elective procedures who are at high risk of PONV.

"Tens of millions of Americans undergo surgery each year and many suffer with nausea and vomiting after their operation," said Peter Kranke, M.D., Professor of Anaesthesiology at the University of Würzburg in Germany and the trial's lead investigator. "PONV contributes to patient distress, can delay recovery after surgery and increases hospital costs. Patients with multiple risk factors for PONV require a multimodal approach for its prevention, including using a combination of anti-nausea drugs with different mechanisms of action, since it cannot be predicted which pathway(s) will be active in a patient."

Risk factors for PONV ("Apfel risk factors") include being female, having a prior history of PONV or motion sickness, non-smokers and those expected to use opioids after surgery for pain. Without effective preventive treatment, nausea and/or vomiting in the 24 hours after surgical operations under anaesthesia may occur in 60 to 80 percent of high-risk patients with three or four of these recognised risk factors.

"International consensus guidelines recommend the use of combinations of antiemetics from different mechanistic classes for the prevention of PONV in high-risk patients, acknowledging the multiple biological pathways that are implicated in PONV," added Dr Gabriel Fox, Acacia Pharma's Chief Medical Officer. "Currently two classes of antiemetics are predominantly used to prevent PONV in these patients: 5HT₃ antagonists (usually ondansetron) and corticosteroids (usually dexamethasone). However, a safe and effective third mechanism antiemetic is required in high-risk patients or those where the act of retching and vomiting may be detrimental to their clinical progress such as upper GI surgery. The clinical results we have seen with BAREMSIS (a dopamine

antagonist) across our extensive Phase 3 development programme, provide strong evidence that BAREMSIS has the potential to fulfil this need."

Professor T.J. Gan, Chair of the Department of Anesthesiology of Stony Brook School of Medicine and Co-Founder and Past President of the American Society of Enhanced Recovery (ASER), commented: "Even when multiple antiemetics are used for prophylaxis, there is still an appreciable failure rate in highest-risk patients. The option to add BAREMSIS to current therapy could be valuable in reducing the incidence of PONV and enhancing patient recovery after surgery. This is a key part of delivering optimal post-operative outcomes in the United States."

Summary of the trial and results

The Phase 3 study was a double-blind, randomised, placebo-controlled trial at 29 sites in France, Germany and the US. It included 1,147 adult patients undergoing elective surgery under general anaesthesia, who had three or four Apfel risk factors. Patients all received one standard antiemetic (approximately half received ondansetron and half dexamethasone) and were randomly assigned to receive in addition either 5 mg of BAREMSIS intravenously (572 patients) or a matching placebo (575 patients), prior to their surgery.

The researchers found 57.7% of patients receiving BAREMSIS had a complete response - defined as no vomiting or need for medication to relieve nausea - in the 24 hours after surgery, compared with 46.6% of those receiving the placebo ($P < 0.001$).

A benefit of BAREMSIS over placebo was seen in both three- (62% vs 54.3%, $P = 0.013$) and four-risk factor patients (50.8% vs 36.7%, $P < 0.001$) and when combined with either a corticosteroid or ondansetron.

Overall, vomiting (13.8% vs. 20%), any nausea (50% vs. 58.3%), significant nausea (37.1% vs. 47.7%), and those requiring fast-acting medication to relieve vomiting (40.9% vs. 49.4%) were significantly lower in the BAREMSIS group. Adverse events occurred no more frequently with BAREMSIS than with placebo.

Reference

[Kranke, P. et al. Amisulpride Prevents Postoperative Nausea and Vomiting in Patients at High Risk. Anesthesiology \(2018\)](#)

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About BAREMSIS®

BAREMSIS comprises a low dose intravenous formulation of the marketed dopamine antagonist amisulpride, which Acacia Pharma has developed for the completely new, patent-protected use of management of PONV.

Data generated by Acacia Pharma indicate that BAREMSIS is an effective, safe dopamine antagonist that can treat established PONV and prevent PONV from occurring, when used alone or in combination with other antiemetics. The Company believes that BAREMSIS can be used:

- to rescue patients who develop PONV despite having received prior standard of care PONV prophylaxis (5HT₃ antagonist and corticosteroid, alone or in combination), and
- prophylactically to prevent PONV in combination with standard of care (5HT₃ antagonist and/or corticosteroid) in the highest risk patients.

A New Drug Application (NDA) submission for BAREMSIS, including data from four positive Phase 3 studies and more than 3,300 surgical patients and healthy volunteers, is currently under review by the US Food and Drug Administration (FDA). Under the Prescription Drug User Fee Act (PDUFA), the FDA has set a target date of 5 October 2018 to complete its review.

About PONV

PONV is a common complication of surgery, occurring in approximately 30% of surgical patients and up to 80% of high-risk patients. It is associated with the use of anaesthetic gases and opioid pain-killers and is particularly common following gynaecological, abdominal, breast, eye and ear operations, especially those lasting an hour or more.

The Group estimates that approximately 65 million surgical procedures are conducted in the US each year that require injectable analgesia and are eligible for antiemetic use to prevent PONV. Based on market research, Acacia Pharma estimates that the total market in the US for prophylactic and rescue treatment comprises an estimated 34 million treatment events annually.

PONV has been ranked as the most undesirable of all surgical complications by patients and contributes significantly to patient anxiety and distress. PONV can delay hospital discharge; result in re-admission after in-patient procedures; and lead to day-case patients being admitted to hospital, all of which can result in significantly increased healthcare costs.

About Acacia Pharma

Acacia Pharma is a hospital pharmaceutical company focused on the development and commercialisation of new nausea & vomiting treatments for surgical and cancer patients. The Group has identified important and commercially attractive unmet needs in nausea & vomiting and has discovered two product candidates based on the same active ingredient, amisulpride, to meet those needs.

The Group's lead project, BAREMSIS for post-operative nausea & vomiting (PONV), has generated positive results in Phase 3 clinical studies and an NDA has been accepted for filing by the US FDA for marketing approval. Its sister project, APD403 for chemotherapy induced nausea & vomiting (CINV) has successfully completed one proof-of-concept and one Phase 2 dose-ranging study in patients receiving highly emetogenic chemotherapy.

Acacia Pharma is based in Cambridge, UK and its US operations are centred in Indianapolis, IN. The Company is listed on the Euronext Brussels exchange under the under ISIN code GB00BYWF9Y76 and ticker symbol ACPH. www.acaciapharma.com

Forward looking statement

This announcement includes forward-looking statements, which are based on current expectations and projections about future events. These statements may include, without limitation, any statements preceded by, followed by or including words such as "believe", "expect", "intend", "may", "plan", "will", "should", "could" and other words and terms of similar meaning or the negative thereof. Forward-looking statements may and often do differ materially from actual results. These forward-looking statements are subject to risks, uncertainties and assumptions about the Company and its subsidiaries and investments, including, among other things, the development of its business, trends in its operating industry, and future capital expenditures and acquisitions. By their

nature, forward-looking statements involve risk and uncertainty because they relate to future events and circumstances. Any forward-looking statements reflect the Company's current view with respect to future events and are subject to risks relating to future events and other risks, uncertainties and assumptions relating to the Group's business, results of operations, financial position, prospectus, growth or strategies and the industry in which it operates. Save as required by law or applicable regulation, the Company and its affiliates expressly disclaim any obligation or undertaking to update, review or revise any forward-looking statement contained in this announcement whether as a result of new information, future developments or otherwise. Forward-looking statements speak only as of the date they are made