

## Press release

# Braeburn Pharmaceuticals and Camurus Announce Positive Top-line Phase 3 Results for Long-acting Buprenorphine (CAM2038) for Treatment of Opioid Addiction

- *Head-to-head study of CAM2038 versus daily sublingual buprenorphine*
- *CAM2038 met both FDA and EMA primary endpoints of non-inferiority ( $p < 0.001$ )*
- *CAM2038 demonstrated statistical superiority for the key secondary endpoint ( $p = 0.004$ )*
- *Robust clinical data to support MAA and NDA submissions in mid-2017*
- *The CAM2038 development program targets an urgent and growing opioid crisis in the US and globally*

**Princeton, New Jersey and Lund, Sweden — 14 November 2016** — Braeburn Pharmaceuticals and Camurus (NASDAQ STO: CAMX) are pleased to announce positive top-line results from a pivotal Phase 3 randomized, double-blind, double-dummy, active controlled trial of weekly and monthly injections of buprenorphine (CAM2038) for treatment of moderate-to-severe opioid use disorder. In addition to achieving the primary endpoint of non-inferiority versus daily sublingual buprenorphine/naloxone (SL BPN/NX, current Standard of Care), CAM2038 also demonstrated superiority for the key secondary endpoint.

"We are pleased with these significant clinical trial results, which show that our CAM2038 injectable buprenorphine products, if approved, can provide effective new solutions for patients and physicians," said Behshad Sheldon, President and CEO of Braeburn Pharmaceuticals. "Opioid addiction is an overwhelming public health epidemic. In the United States alone, there are 2.6 million patients diagnosed with opioid addiction, and approximately 30,000 people die every year from opioid overdoses. CAM2038 comes in both weekly and monthly formulations, each in a range of dosage strengths, in alignment with clinical practice of treating opioid addiction, where different patients have different and evolving needs as they progress from treatment initiation to stabilization and eventually long-term maintenance. We believe that our CAM2038 products, together with our recently approved Probuphine 6-month buprenorphine implant, have the potential to transform the treatment of opioid addiction."

In the Phase 3 study enrolling 428 patients with opioid use disorder, CAM2038 achieved the main objective of statistical non-inferiority compared to the active comparator of SL BPN/NX for both the FDA and the EMA specified endpoints of responder rate (RR) (CI -3.5%, 10.4%;  $p < 0.001$ ) and percent negative urine samples for opioids (CI -0.2%, 13.7%;  $p < 0.001$ ), respectively.



Importantly, while this Phase 3 study was designed and powered for assessing non-inferiority, the protocol also planned to test superiority against SL BPN/NX based on the pre-defined secondary endpoint of cumulative distribution function (CDF) of the percent urines negative for opioids combined with self-reports for weeks 5 through 24. The superiority of CAM2038 over SL BPN/NX was established with  $p=0.004$ .

The retention rate in the trial was approximately 57.5% and, as expected, similar across both treatment arms. The overall safety profiles were comparable between the two treatment groups, with few serious adverse events (SAE's) reported for the CAM2038 and SL BPN/NX (3.2% vs 6.0%, respectively). There were no reported overdoses in the CAM2038 arm compared to 4 non-fatal overdoses (3 on heroin, one on Klonopin) in the SLBPN/NX arm. Injection site reactions occurred in 19% of the CAM2038 participants vs 22% of the SL BPN/NX participants. Seventy-four percent of the injection site reactions were reported as mild, 26% as moderate, and none were reported as severe.

"The positive results of this pivotal head-to-head Phase 3 study represent an important breakthrough for our weekly and monthly CAM2038 products for treatment of opioid dependence, as well as a confirmation of the strength and applicability of our proprietary FluidCrystal® technologies and pipeline," said Dr. Fredrik Tiberger, President and CEO of Camurus. "The results of this rigorous evaluation of CAM2038 compared to standard of care provide strong support for our upcoming market authorization applications. The demonstrated robust treatment effect of CAM2038 versus daily sublingual buprenorphine further underscores the potential to significantly improve treatment outcomes, in addition to avoiding the complications and risks associated with current daily medications."

Given the successful results from this pivotal Phase 3 trial and the previously reported Phase 2 opioid challenge study, Braeburn and Camurus look forward to working expeditiously with the FDA and EMA to begin the submission process to bring this potentially transformative new treatment to the many patients living with opioid use disorder in the US, Europe and other parts of the world. The FDA has granted Fast Track designation for CAM2038 subcutaneous injectable products for the treatment of opioid addiction.

"A weekly buprenorphine injection would be an attractive option for initiation, early treatment, and treatment of unstable patients, where weekly medical visits are common, whereas a monthly injection is an attractive option for longer term maintenance treatment where monthly visits are common practice," said Dr. Edward Nunes, MD, Professor of Psychiatry at Columbia University Medical Center and Investigator in the study."

According to Dr. Michelle Lofwall, Assoc. Professor of Behavioral Science and Psychiatry at the University of Kentucky Center on Drug and Alcohol Research and Primary Investigator in the study, "If approved, the CAM2038 weekly and monthly injectable buprenorphine medications can improve how we treat opioid addiction and decrease the stigma associated with the medication that is in large part due to concerns about non-adherence and diversion. Together with the six-month buprenorphine implant, these new long-acting medication delivery systems would allow us to administer a proven medication to the patients directly, ensuring adherence which leads to improved medication efficacy as demonstrated in this trial as well as avoiding the potential for missed or stolen doses, diversion or accidental pediatric exposure, which are significant public health concerns."



“Buprenorphine is a remarkably efficacious medication for treatment of opioid dependence, but in practice its effectiveness is limited by poor adherence” added Dr. Nunes. It is all too easy for patients to miss daily doses of buprenorphine pills or strips, and then relapse. A long-acting injection, such as CAM2038, circumvents the need for daily pill taking and has the potential to substantially improve adherence and treatment outcome. In our experience, the CAM2038 injections were easy to administer and well tolerated by patients. It should be easy to implement in a wide range of office, clinic, or hospital based practices.”

### **About the Phase 3 trial**

*The present Phase 3 trial was a multicenter, randomized, double blind, double dummy, active controlled study that enrolled a total of 428 patients at 36 US sites with moderate to severe opioid use disorder (DSM–5 criteria; American Psychiatric Association, 2013).*

*To meet enrollment criteria, participants could not be receiving treatment at the start of the study, but were seeking medication assisted treatment for opioid use disorder. Following randomization, participants underwent initiation with buprenorphine (BPN) treatment with either sublingual SL BPN/NX tablets (Group 1) or with CAM2038 q1w (Group 2). This is the first Phase 3 trial where patients are initiated with an injectable buprenorphine product, after a single oral test sublingual tablet, and without the benefit of a “stabilization phase”. After one week, Group 1 continued with daily SL BPN/NX and Group 2 with weekly CAM2038 for the following 11 weeks (Phase 1). Subjects were then transitioned to Phase 2 for the subsequent 12 weeks whereby Group 1 continued daily treatment with SL BPN/NX, while subjects in Group 2 (previously receiving weekly CAM2038 q1w) were switched to monthly injections with CAM2038 q4w.*

*The primary objective of this trial was to demonstrate the non-inferiority (NI) of CAM2038 compared with sublingual buprenorphine among adult patients with Opioid Use Disorder. The primary efficacy variable used for FDA was the responder rate in both Phase 1 and 2 of the trial. To be a responder for Phase 1, the patient must have had no evidence of illicit opioid use at Week 12 and have no evidence of illicit opioid use for at least two out of the three weeks from Week 9 to Week 11, inclusive. To be a responder for Phase 2, the patient must have demonstrated no evidence of illicit opioid use at Month 6 and no evidence of illicit opioid use in five out of the six illicit opioid use assessments in Phase 2. To meet the definition of a responder for the full trial, participants needed to meet responder criteria for both Phases 1 and 2. The primary efficacy variable used for EMA was mean percent of urines negative for opioids. The trial's key secondary efficacy endpoint was a superiority testing of the cumulative distribution function (CDF) of urine samples negative for illicit opioids, verified with self-report.*

*The overall safety profile was comparable between the two treatment groups, with few serious adverse events (SAE's) reported for the CAM2038 and SL BPN/NX (3.2% vs 6%, respectively). There were no reported overdoses in the CAM2038 arm, compared to 4 overdoses in the SL BPN/NX. There was one death due to a traffic accident in the CAM2038 arm. Complete results of the study will be presented at an upcoming scientific conference.*

### **About Opioid Use Disorder (OUD) and Treatment**

*Opioid-involved overdose deaths are a public health epidemic, resulting in about 30,000 deaths in the United States in 2015. These deaths were caused by prescription-drug misuse and a rise in heroin use (twenty and ten thousand respectively). Opioids kill more people than firearms and car accidents. In Europe, it is estimated that over 70,000 lives*



were lost to drug overdoses in Europe in the first decade of the twenty-first century. Reducing drug-related deaths therefore remains a major challenge for public health policy.

12.5 million people misused opioid pain relievers and over 800,000 people used heroin in the United States in 2015. In 2013, prescription opioid abuse accounted for an estimated \$78.5 billion in U.S. health and social costs. Despite the extreme high social costs and large patient population with opioid addiction, only about half of the estimated 2.6 million and 1.3 million people diagnosed with opioid addiction in the United States and Europe receive treatment medication.

Opioid use disorder is diagnosed by signs and symptoms of compulsive and harmful (psychologically, socially, physically) ongoing use of opioids even when there is a strong desire to cease their use. Cravings or desire for use and painful opioid withdrawal symptoms can be overwhelming. There are clear changes in the brain involved with cognition, memory, rewards in both conscious and unconscious circuits that underlie opioid addiction.

Buprenorphine maintenance treatment is currently considered a gold standard for opioid use disorder treatment with more than one million patients receiving buprenorphine in the US and Europe. The medication reduces craving, reduces the risk of relapse, reduces fatalities from opioid overdose, and decreases injection drug behaviors associated with spread of infectious diseases such as hepatitis C and HIV. Currently, most patients on buprenorphine take daily doses. These forms of the medication are sometimes misused, abused and diverted or accidentally ingested by children. In addition, patients can inadvertently or intentionally miss doses, which makes them vulnerable to relapse and overdose death.

#### **About CAM2038 Products**

CAM2038 are buprenorphine subcutaneous investigational new drugs in late stage clinical development for the treatment of opioid addiction. Once-weekly and once-monthly formulations have been developed, each with multiple doses, to allow individualized treatment of patients with opioid use disorder as a part of comprehensive treatment plan to include counseling and psychosocial support.

The CAM2038 products are designed for administration by healthcare personnel to ensure proper delivery and medication adherence to minimize the risks of diversion, abuse, misuse, and accidental exposure by children. Previously, the CAM2038 products have been evaluated in four completed Phase 1/2 clinical trials. In addition to the study reported on today, we have two other ongoing clinical trials of CAM2038 in opioid addiction, a 48-week safety trial of weekly and monthly CAM2038 that is being conducted across 29 sites in the United States, Australia and Europe, and a Phase 2 trial to evaluate whether weekly and monthly CAM2038 can be expected to produce similar buprenorphine blood levels following administration at various injection sites. So far, more than 900 subjects have been enrolled in clinical studies evaluating CAM2038.

Design attributes of CAM2038 include small dose volumes of maximum about 0.6 mL (for the highest weekly dose) filled in prefilled syringes with a thin 23 gauge injection needle and administered subcutaneously, intended to minimize discomfort for patients, leading to enhanced patient and physician acceptance. CAM2038 is stored at room temperature, therefore avoiding the need for cold chain distribution and refrigerator storage, which



most healthcare provider offices do not have. As CAM2038 is provided ready for use in a prefilled syringe, no mixing steps or room temperature conditioning is required.

#### **About Braeburn Pharmaceuticals**

*Braeburn Pharmaceuticals, an Apple Tree Partners company, is a commercial-stage pharmaceutical company delivering individualized medicine in neuroscience. Long-acting therapeutic treatment options can be essential to improving patient outcomes and facilitating recovery in neurological and psychiatric disorders, which are often complicated by stigma and present significant public health challenges. Braeburn's commercial product, Probuphine® (buprenorphine) implant was approved by the FDA in May 2016. Braeburn's investigational product pipeline consists of long-acting implantable and injectable therapies for serious neurological and psychiatric disorders, including opioid addiction, pain, and schizophrenia. Braeburn's pipeline products are at various stages of clinical development and include CAM2038 weekly and monthly subcutaneous injection depot formulations of buprenorphine, being investigated in opioid addiction and pain, BB0417 buprenorphine/granisetron injectable for acute pain, and BB0817, six-month risperidone implant being investigated in schizophrenia. More information on Braeburn can be found at [www.braeburnpharmaceuticals.com](http://www.braeburnpharmaceuticals.com).*

#### **About Camurus**

*Camurus is a Swedish research-based pharmaceutical company committed to developing and commercialising innovative and differentiated medicines for the treatment of severe and chronic conditions. New drug products with best-in-class potential are conceived based on the proprietary FluidCrystal® drug delivery technologies and an extensive R&D expertise. Camurus' clinical pipeline includes products for treatment of cancer, endocrine diseases, pain and addiction, developed in-house and in collaboration with international pharmaceutical companies. The company's share is listed on Nasdaq Stockholm under the ticker "CAMX". For more information, visit [www.camurus.com](http://www.camurus.com).*

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