

The background of the slide is a blurred, blue-tinted photograph of a large crowd of people, likely at a conference or meeting. The people are out of focus, creating a bokeh effect with soft, light-colored spots.

**camurus**<sup>®</sup>

# Annual General Meeting 2019

---

CEO presentation  
Lund, 9 May 2019

## Forward-looking statements

---

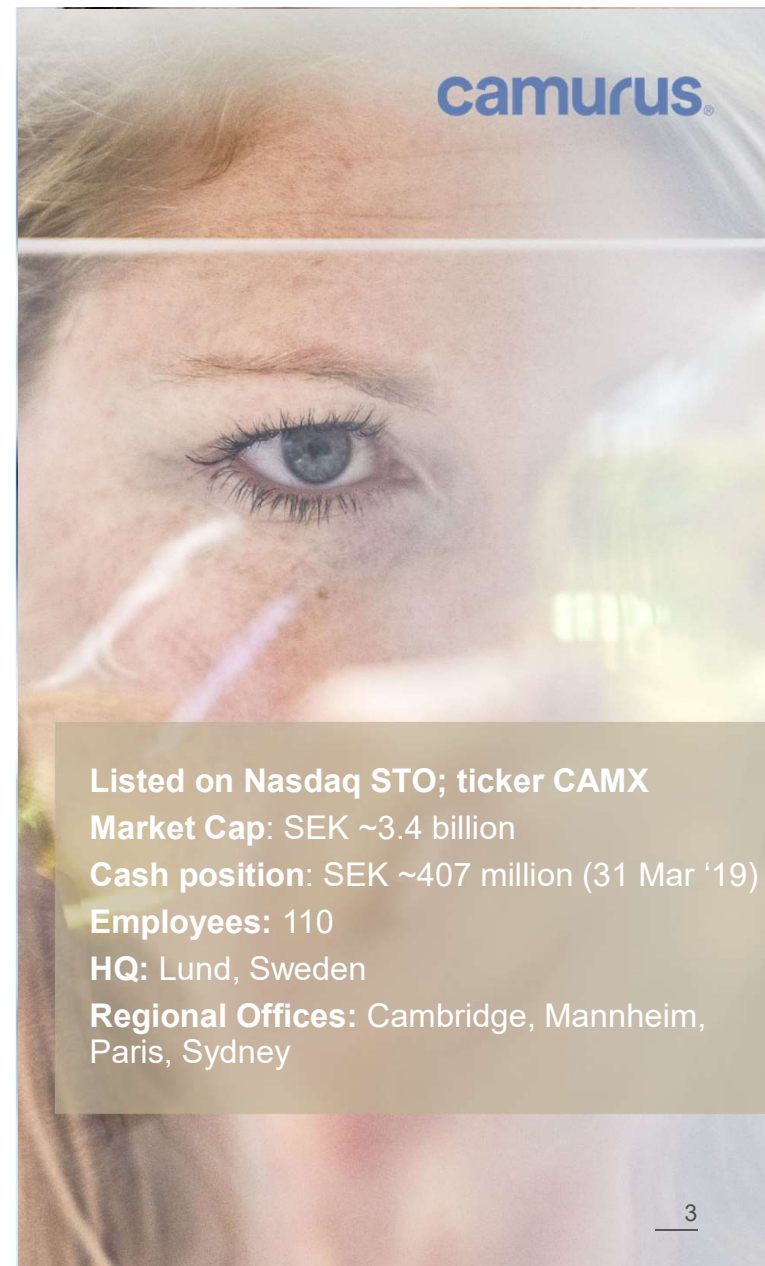
*This presentation contains forward-looking statements that provide our expectations or forecasts of future events such as new product developments and regulatory approvals and financial performance.*

*Camurus is providing the following cautionary statement. Such forward-looking statements are subject to risks, uncertainties and inaccurate assumptions. This may cause actual results to differ materially from expectations and it may cause any or all of our forward-looking statements here or in other publications to be wrong. Factors that may affect future results include currency exchange rate fluctuations, delay or failure of development projects, loss or expiry of patents, production problems, unexpected contract, patent, breaches or terminations, government-mandated or market-driven price decreases, introduction of competing products, Camurus' ability to successfully market products, exposure to product liability claims and other lawsuits, changes in reimbursement rules and governmental laws and interpretation thereof, and unexpected cost increases.*

*Camurus undertakes no obligation to update forward-looking statements*

# Camurus in brief

<b>Unique FluidCrystal® nano-technologies</b>	<ul style="list-style-type: none"> <li>• In-house developed with strong IP</li> <li>• New generation long-acting depot technology</li> <li>• Validated in 20 clinical trials and by approved products</li> </ul>
<b>Broad, late-stage R&amp;D pipeline</b>	<ul style="list-style-type: none"> <li>• 10 clinical programs in addiction, pain, oncology, endocrinology, obesity and CV</li> </ul>
<b>Approved commercial products</b>	<ul style="list-style-type: none"> <li>• Weekly and monthly Buvidal® approved in the EU and Australia for treatment of opioid dependence</li> </ul>
<b>Own commercial organization</b>	<ul style="list-style-type: none"> <li>• Fully operational for Buvidal® EU launch, initiated in Finland, Sweden, the UK, Germany, and Denmark</li> </ul>
<b>Partnerships</b>	<ul style="list-style-type: none"> <li>• Braeburn Pharmaceuticals, Rhythm, Solasia Pharma, Medison...</li> </ul>
<p><b>Experienced management and dedicated teams</b></p>	



**Listed on Nasdaq STO; ticker CAMX**  
**Market Cap:** SEK ~3.4 billion  
**Cash position:** SEK ~407 million (31 Mar '19)  
**Employees:** 110  
**HQ:** Lund, Sweden  
**Regional Offices:** Cambridge, Mannheim, Paris, Sydney

# 2018 operating performance and pipeline progress





## PIPELINE PROGRESS

## OPERATIONAL HIGHLIGHTS

	PIPELINE PROGRESS	OPERATIONAL HIGHLIGHTS
2018	<ul style="list-style-type: none"> <li>✓ Buvidal® approved in both the EU and Australia</li> <li>✓ Brixadi™ received tentative approval in the US</li> <li>✓ Publication of Buvidal® Ph. 3 results in JAMA Int. Med.</li> <li>✓ Positive CAM2038 Phase 3 results in chronic pain</li> <li>✓ Positive Phase 1 SAD and MAD results for CAM2043</li> <li>✓ Publication of Phase 2 results for CAM2029</li> <li>✓ Phase 1b clinical milestone in Rhythm collaboration</li> </ul>	<ul style="list-style-type: none"> <li>✓ Commercialization infrastructure in the EU and Australia</li> <li>✓ Commercial manufacturing of Buvidal®</li> <li>✓ Supply and distribution chain in place</li> <li>✓ Launch platform established</li> </ul>
2019	<ul style="list-style-type: none"> <li>✓ Court proceedings initiated by Braeburn to overturn a market exclusivity, and seeks immediate US market approval of Brixadi®</li> </ul>	<ul style="list-style-type: none"> <li>✓ EU Buvidal® launch initiated in Finland, Sweden, the UK, Germany and Denmark</li> <li>✓ MSEK 403 Rights Issue completed</li> </ul>

**Clinically documented compounds**  
**+**  
**FluidCrystal® technology**

# Advancing product pipeline

PRODUCT	PHASE 1-2	PHASE 3	REGISTRATION	MARKET	
Buvidal® q1w OPIOID DEPENDENCE				MARKET	
Buvidal® q4w OPIOID DEPENDENCE				MARKET	
Brixadi® q1w OPIOID DEPENDENCE - BRAEBURN <sup>1</sup>			TENTATIVE APPROVAL		
Brixadi® q4w OPIOID DEPENDENCE - BRAEBURN <sup>1</sup>			TENTATIVE APPROVAL		
CAM2038 q1w CHRONIC PAIN <sup>1</sup>		PHASE 3			
CAM2038 q4w CHRONIC PAIN <sup>1</sup>		PHASE 3			
CAM2029 ACROMEGALY	PHASE 1-2				
CAM2029 NEUROENDOCRINE TUMORS	PHASE 1-2				
CAM2032 PROSTATE CANCER	PHASE 1-2				
CAM4072 GENETIC OBESITY DISORDERS - RHYTHM <sup>2</sup>	PHASE 1-2				
CAM2043 PULMONARY ARTERIAL HYPERTENSION	PHASE 1-2				
CAM2047 CINV <sup>3</sup>	PHASE 1-2				
CAM2048/58 POSTOPERATIVE PAIN & PONV <sup>4</sup> - BRAEBURN <sup>1</sup>	PHASE 1-2				

1. Braeburn holds the rights to North America; 2. Developed by Rhythm Pharmaceuticals under a worldwide license to FluidCrystal®; 3. Chemotherapy-induced nausea and vomiting; 4. Postoperative nausea and vomiting;



## Buvidal®/Brixadi™

---

Weekly and monthly  
buprenorphine depots

Game-changer in opioid  
dependence treatment

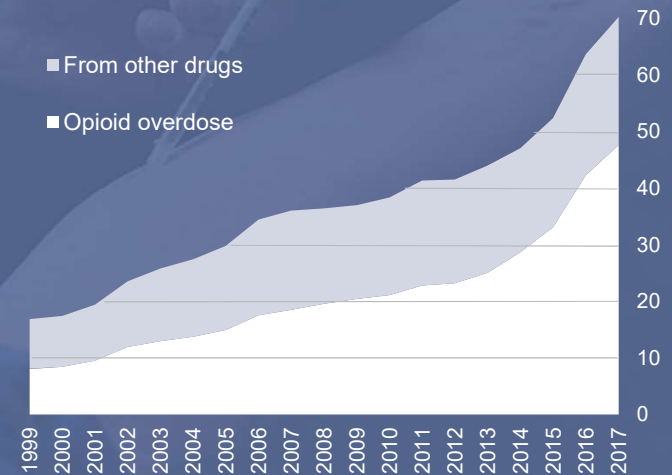
# Opioid dependence – escalating global health crisis

- Largest society burden of all drugs<sup>1</sup>
- 34 million opioid users worldwide<sup>1</sup>
- High need for better access to care and new treatment alternatives
- Investment in treatment brings substantial value and saves lives
- Significant limitation with current daily medications

Source: 1. UNODC, World Drug Report 2017; 2. Center for Disease Control & Prevention 2018; 3. Frazier et al, 2017, Journal of the American Medical Association; 4. Crow D. Financial Times.com, accessed on March 13, 2018, <https://www.ft.com/content/d22e742c-e65c-11e7-97e2-916d4fbac0da>

camurus®

Mounting US opioid overdose deaths<sup>2</sup>  
(thousands)



#1 cause of death for people under 50 in the US

30:1 non-fatal to fatal overdoses<sup>3</sup>

Recent US life expectancy decline largely due to opioids<sup>4</sup>



# Buvidal® – first long-acting injection treatment of opioid dependence in the EU and Australia

- Buvidal® is indicated (EU) **for treatment of opioid dependence** within a framework of medical, social and psychological treatment in adults and adolescents from 16 years
- **Individualized dosing** for use across treatment phases: initiation, switching from daily medications and long-term maintenance treatment
- **Superiority versus daily standard treatment** with daily buprenorphine/naloxone included in clinical outcomes
- **Removes burdens and stigma** of daily medication
- **HCP administration safeguards** against diversion, misuse and pediatric exposure



## Buvidal brings unique values to patients and HCPs

PRODUCT	WEEKLY DOSING	MONTHLY DOSING	MULTIPLE DOSES	CHOICE OF INJECTION SITES	SMALL NEEDLE	LOW VOLUMES	ROOM TEMP. STORAGE	DAY ONE INITIATION	CLIN. DATA VS ACTIVE CONTROL*
<small>Weekly/Monthly</small> <b>Buvidal</b> <sup>®</sup> <small>BUPRENORPHINE            PROLONGED-RELEASE            SOLUTION FOR INJECTION</small>	✓	✓	✓	✓	✓	✓	✓	✓	✓
<small>ONCE-MONTHLY</small> <b>Sublocade</b> <sup>™</sup> <small>(buprenorphine extended-release)            injection for subcutaneous use &amp;            100mg-300mg</small>	—	✓	—	—	—	—	—	—	—
<b>Vivitrol</b> <sup>®</sup> <small>(naltrexone for extended-release            injectable suspension)</small>	—	✓	—	—	—	—	—	—	—

\*Studies referenced in product labels

# Strong clinical data for Buvidal® versus daily standard treatment

**Non-inferior and Superior** efficacy demonstrated in pivotal Phase 3 study versus standard daily SL BPN/NX<sup>1</sup>

**High Treatment Retention** ~70% at 48 weeks<sup>2</sup>

**Blockade of Opioid Effects** from the first dose<sup>3</sup>

**Effective suppression** of withdrawal and cravings<sup>1,2,3</sup>

**Safety Profile** comparable to SL BPN/NX except for mild and moderate injection site reactions<sup>1,2</sup>

**No Opioid Overdoses** reported across clinical studies for participants treated with Buvidal®<sup>1,2,3,4,5</sup>

**High Patient Satisfaction** including versus SL BPN<sup>2</sup>

<sup>1</sup>Lofwall et al. JAMA Int. Med. 2018;178(6): 764-773; <sup>2</sup>Frost et al. Addiction, 2019 in press, <sup>3</sup>Walsh et al, JAMA Psychiatry 2017;74(9):894-902; <sup>4</sup>Haasen, C, et al, J Subst Abuse Treat. 2017;78:22-29; <sup>5</sup>Albayaty M, et al, Adv Ther. 2017 34(2):560-575; <sup>6</sup>SL BPN sublingual buprenorphine/naloxone

## Key publications

Research

JAMA Internal Medicine | Original Investigation

**Weekly and Monthly Subcutaneous Buprenorphine Depot Formulations vs Daily Sublingual Buprenorphine With Naloxone for Treatment of Opioid Use Disorder**  
A Randomized Clinical Trial

Michelle R. Lofwall, MD, Sharon L. Walsh, PhD, Edward V. Nunes, MD, Genie L. Bailey, MD, Stacey C. Sigmon, PhD, Kyle M. Kampman, MD, Michael Frost, MD, Fredrik Tiberg, PhD, Margareta Linden, PhD, Behshad Sheldon, BS, Sonia Oosman, BS, Stefan Peterson, PhD, Michael Chen, PhD, Sonnie Kim, PharmD

JAMA Psychiatry | Original Investigation

**Effect of Buprenorphine Weekly Depot (CAM2038) and Hydromorphone Blockade in Individuals With Opioid Use Disorder**  
A Randomized Clinical Trial

Sharon L. Walsh, PhD, Sandra D. Comer, PhD, Michelle R. Lofwall, MD, Bradley Vince, DO, Naama Levy-Cooperman, PhD, Debra Kelsch, MD, Marion A. Coe, BA, Jermaine D. Jones, PhD, Paul A. Nuzzo, MA, Fredrik Tiberg, PhD, Behshad Sheldon, BS, Sonnie Kim, PharmD

Adv Ther  
DOI: 10.1007/s12325-016-0472-9

ORIGINAL RESEARCH

**Pharmacokinetic Evaluation of Once-Weekly and Once-Monthly Buprenorphine Subcutaneous Injection Depots (CAM2038) Versus Intravenous and Sublingual Buprenorphine in Healthy Volunteers Under Naltrexone Blockade: An Open-Label Phase 1 Study**

Muna Albayaty · Margareta Linden · Håkan Olsson · Markus Johnsson · Kerstin Strandgården · Fredrik Tiberg

Pharmacokinetics and pharmacodynamics of a buprenorphine subcutaneous depot formulation (CAM2038) for once-weekly dosing in patients with opioid use disorder

Christian Haasen <sup>1</sup>, Margareta Linden <sup>2</sup>, Fredrik Tiberg <sup>3,4,5</sup>

<sup>1</sup> Clinical Trial Center North, Medicines GmbH, University Medical Center Hamburg Eppendorf, Martinistraße 52, Haus 516, 20246 Hamburg, Germany  
<sup>2</sup> Camurus AB, Ribon Science Park, Gamma Building, Solvegatan 41, 223 79 Lund, Sweden

Contents lists available at ScienceDirect

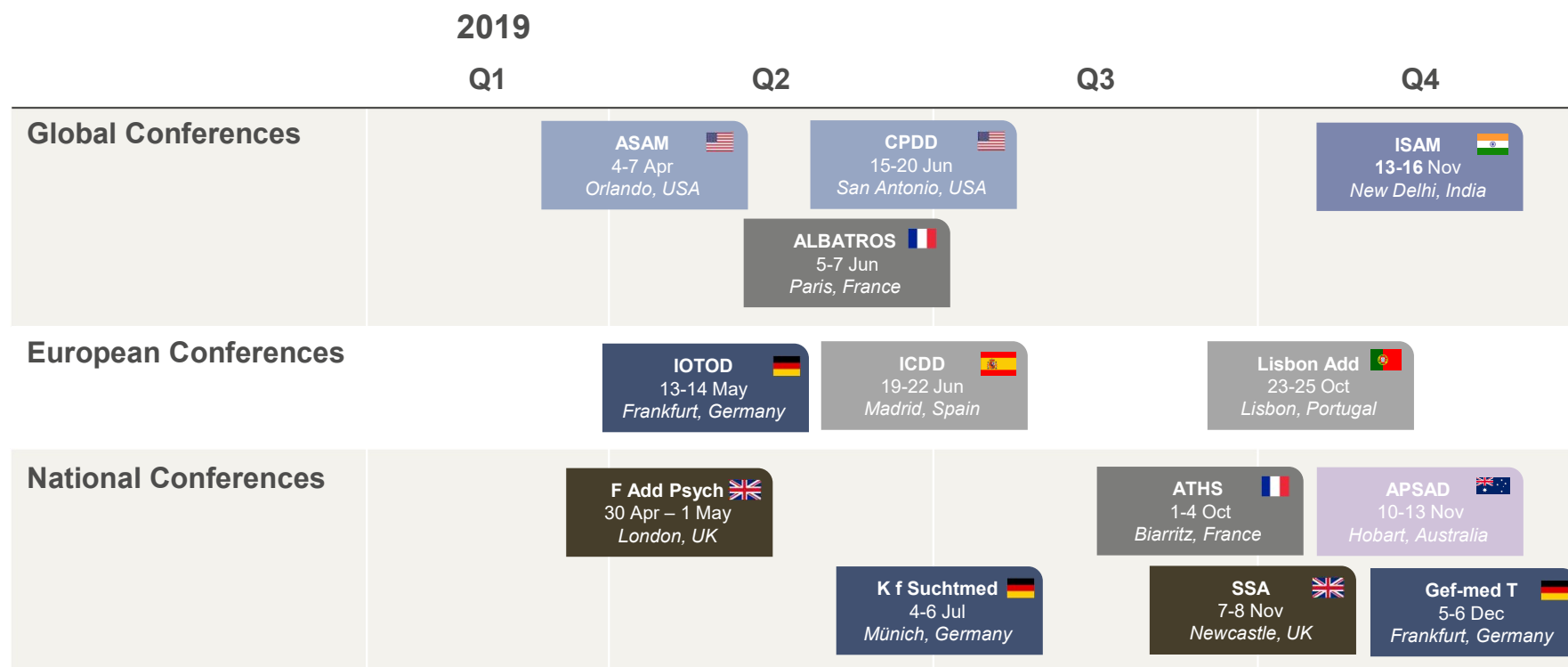
Journal of Substance Abuse Treatment

Pharmacokinetics and pharmacodynamics of a buprenorphine subcutaneous depot formulation (CAM2038) for once-weekly dosing in patients with opioid use disorder

Christian Haasen <sup>1</sup>, Margareta Linden <sup>2</sup>, Fredrik Tiberg <sup>3,4,5</sup>

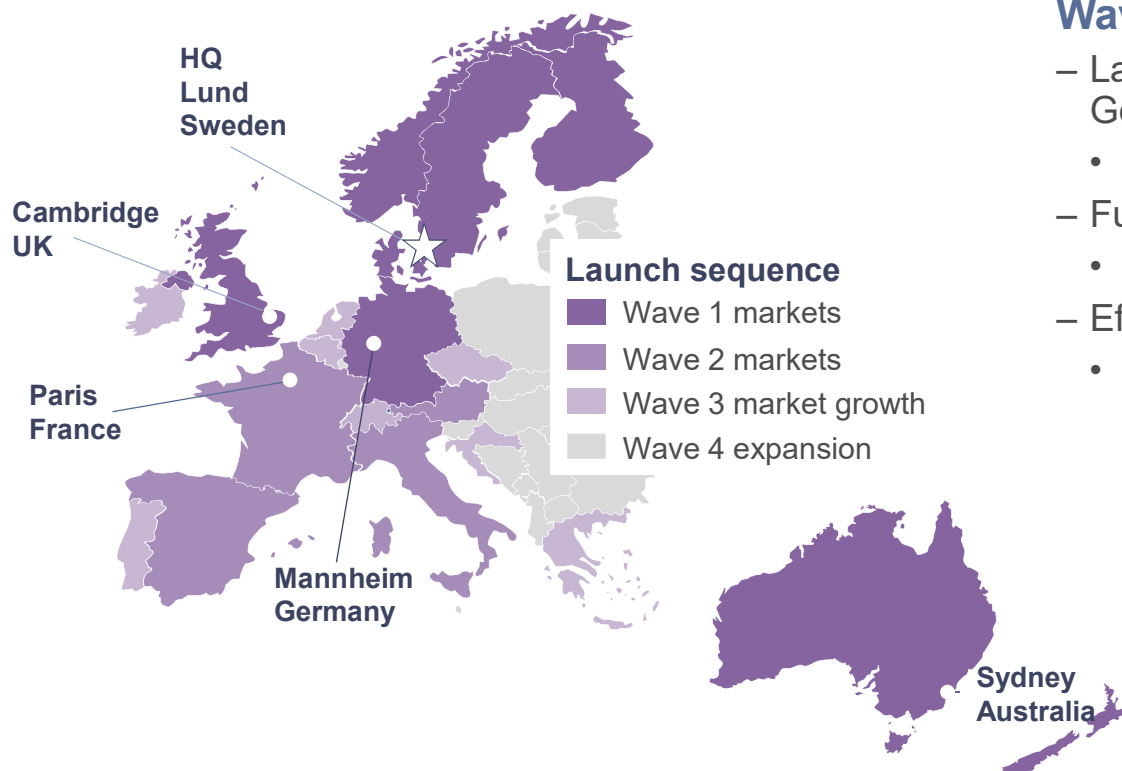
<sup>1</sup> Clinical Trial Center North, Medicines GmbH, University Medical Center Hamburg Eppendorf, Martinistraße 52, Haus 516, 20246 Hamburg, Germany  
<sup>2</sup> Camurus AB, Ribon Science Park, Gamma Building, Solvegatan 41, 223 79 Lund, Sweden

# Buvidal® scientific communication and dissemination of data at scientific conferences during 2019





# Buvidal® EU launch initiated



## Wave 1 markets

- Launched in Finland, Sweden, the UK, Germany and Denmark from January to March 2019
  - Norway and Australia Q2
- Fully operative M&S teams in place on all markets
  - 65 heads, >80% customer facing
- Effective supply and distribution
  - Delivery to clinic <24h.

## Wave 2 markets

- Market access and medical education
  - Pricing & reimbursement
- Key functions onboarded (10 heads)
  - Austria, Spain, Italy, France target launches from Q3 '19 to Q1 '20
  - Israel – Medison Q1 '20

## Case story Finland – first launch market Q1 2019

### Status April 2019

- ~ 210 Buvidal patients
  - New to treatment
  - Conversion from sublingual buprenorphine, both from film and tablets
  - Some conversions from methadone
- ~ 10% buprenorphine market share
- ~ 6% of total treated patients

### Observations

- High initial retention
  - less than 10 patients (<5%) have dropped out since launch
- High acceptance by patients
- Most patients currently on weekly depot
- No reported overdoses

*“Buvidal gives patients freedom to concentrate on life and recovery, instead of their medication”*  
 Antti Mikkonen MD, CEO & Medical Director, Addiktum Oy



## Building on positive 12-week Buvidal® experience

---

### Positive anecdotal feedback from HCPs

- Buvidal® is easy to administer
- Ability to individualize Buvidal® dosing is important
- So far, high treatment retention

### and from patients

- Daily fluctuation and withdrawal ceased and patients feel stable all the time
- No anxiety or worries of missing, forget or loose their medicine
- Less burden and more freedom

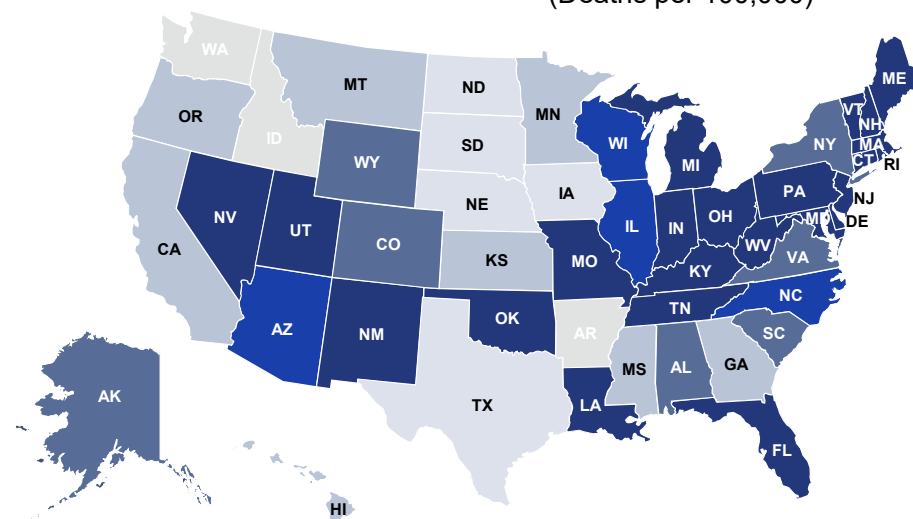
### Key ongoing activities

- Continued medical education to share evidence base and practical implementation of Buvidal®
- Ensuring formulary inclusion and funding release
- Driving HTA review processes
- Supporting local treatment models and guidelines
- In wave 2 markets, accelerating KOL engagement and distribution set-up

## Making Brixadi™ available to US patients

- **Tentative approval Brixadi™ on 21 Dec. 2018**
- **Final approval of monthly product subject to the expiration of an exclusivity period until November 2020 – unless earlier resolved**
- **Brixadi™ Weekly not blocked by exclusivity** and could be approved and launched separately
- **Braeburn has initiated court proceedings to overturn exclusivity and seeks immediate market approval of Brixadi™ in the US**
  - Court decision expected in Q3 2019

### US overdose deaths 2017<sup>2</sup>





## Pipeline update

---

# CAM2038 chronic pain – completing clinical registration program

**Market opportunity**

- 100 million Americans and 75 million Europeans with chronic pain<sup>1,2</sup>
- Chronic pain estimated to cost US society USD ~600 billion per year<sup>3</sup>

**Medical need addressed**

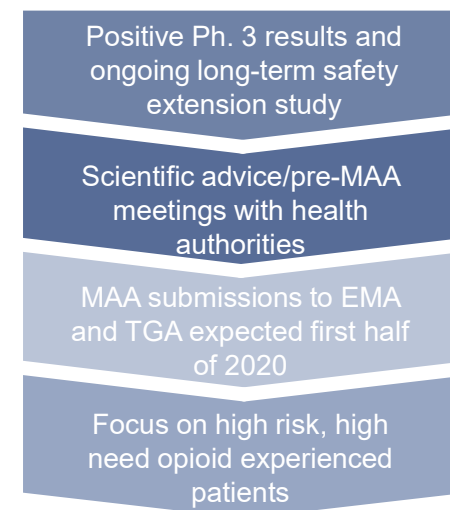
- Effective round-the-clock management of chronic pain, with reduced risk of development of tolerance and dependence
- Mitigation of risks of diversion, misuse and unintended child exposure

**Key clinical results**

- CAM2038 met primary and key secondary Phase 3 endpoints in a pivotal enriched-enrollment and randomized withdrawal study
  - Significantly improved relief of the average and worst pain intensity compared to placebo demonstrated

**Next steps**

- Results and study report from Phase 3 long-term safety study
- Meetings with health authorities in H2 2019
- Regulatory submissions planned in H1 2020

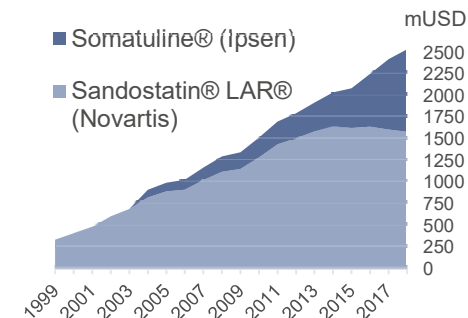


Source: 1. Global Industry Analysts, Inc. report 2011; 2. Pain Practice 2014, 14, 79-94; 3. Gaskin D, Richard P., J. Pain 2012; 13 (8): 715-724

# CAM2029 – Phase 3 program initiation

## Market opportunity

- Somatostatin analogue sales 2018: >USD 2.5 billion<sup>1</sup>
- 20 years of market growth at 20% CAGR
- Long-acting SSA US price-range: \$51,000 to \$146,000 WAC / year<sup>2</sup>



## Medical need addressed

- Enhanced efficacy and response rates in treatment of acromegaly and NET
- Easy and convenient self-administration option

## Key clinical results

- Long-acting octreotide release demonstrated<sup>3</sup>
- High octreotide exposure<sup>3</sup>
- Rapid and sustained suppression of insulin growth factor-1 (IGF-1)<sup>3</sup>
- Well maintained or improved biochemical control indicated in patients with acromegaly<sup>4</sup>
- Well maintained or improved symptom control indicated in NET patients<sup>4</sup>

## Next steps

- **24-week, randomized, placebo controlled Phase 3 study** to assess efficacy and safety of CAM2029 in patients with acromegaly
  - Planned start early Q3 2019
- **52-week, open-label Phase 3 safety and tolerability study** of CAM2029 in patients with acromegaly
  - Planned start in Q3 2019

Source: 1. GlobalData 2019; 2. US weighted average cost for mid-range doses, 20183. Tiberg F, Br J Clin Pharmacol. 2015 Sep;80(3):460-72; 4. Pavel M et al, Cancer Chemotherapy and Pharmacology 2019; 83:375–385

## CAM2043 – preparing for Phase 2

### Market opportunity

- Global market for pulmonary arterial hypertension: >USD 5 billion<sup>1</sup>
- Treprostinil market >USD 1 billion in 2018<sup>1</sup>

### Medical need

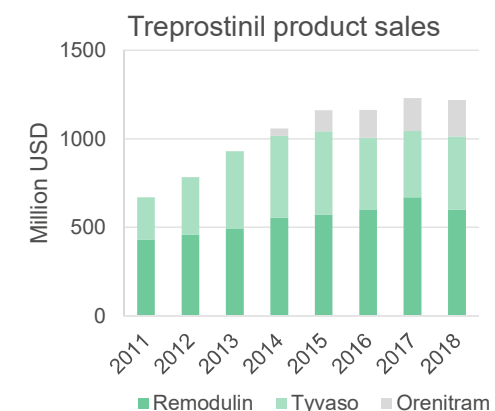
- Complicated handling and risk of infusion related infections with current infusion pump systems
- Complex dosing schedule or sub-efficacious and variable plasma levels with current oral and inhaled products

### Key clinical results

- Positive results from Phase 1 SAD and MAD study with CAM2043 – Dose proportional pharmacokinetics with duration of at least 7 days<sup>2</sup>

### Next steps

- Manufacturing of clinical study material
- Start of Phase 2 study in PAH patients planned in Q4 2019



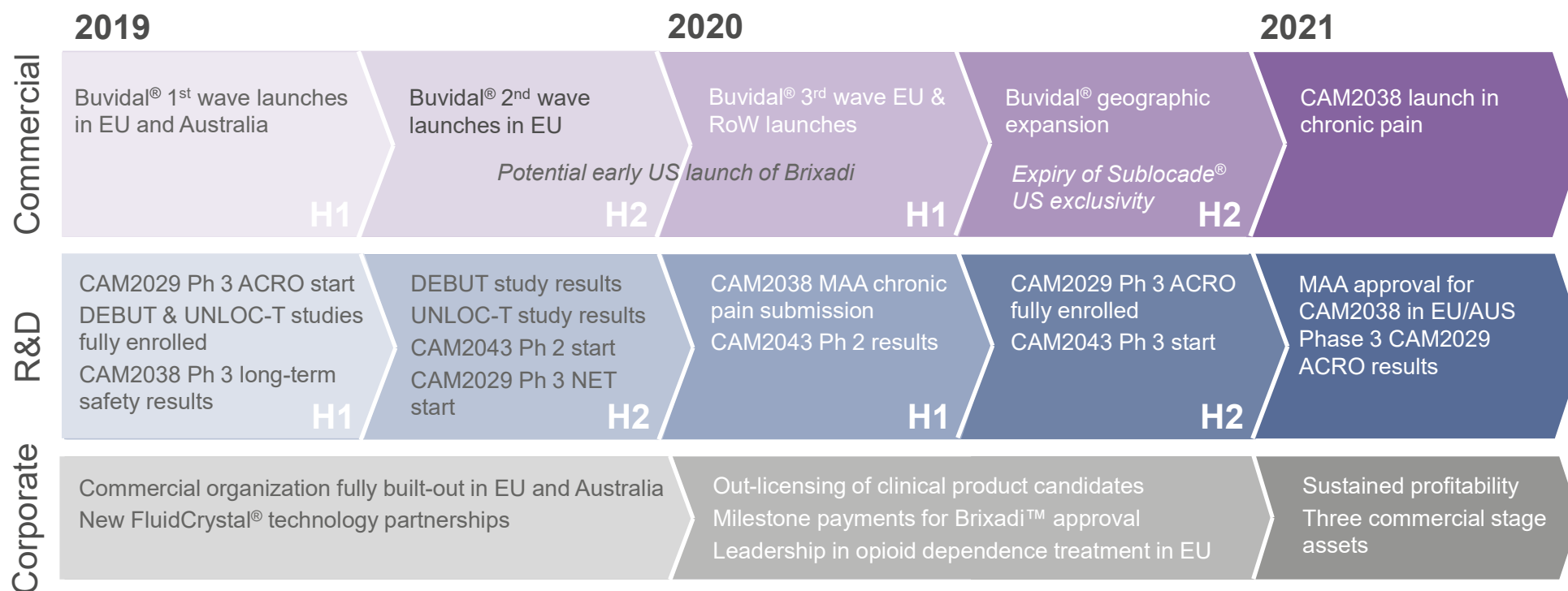


## Multiple levers for growth and value creation

---

<b>Buvidal® / Brixadi™</b>	<ul style="list-style-type: none"> <li>• Establish leadership in opioid dependence treatment with Buvidal® in Europe and Australia</li> <li>• Support US approval and launch of Brixadi™ by Braeburn and continue geographic expansion through partnerships</li> </ul>
<b>Pipeline</b>	<ul style="list-style-type: none"> <li>• Drive late-stage development and regulatory approvals for CAM2038 in chronic pain and CAM2029 in acromegaly and NET</li> <li>• Build and expand our pipeline of innovative drug product candidates for treatment of serious and chronic disease</li> </ul>
<b>Corporate</b>	<ul style="list-style-type: none"> <li>• Strengthen and increase the applicability of our FluidCrystal® technology to new drugs and therapy areas</li> <li>• Develop long-term profitability through own sales, partnerships and business development</li> </ul>

# Outlook to 2021 – strong news flow expected





camurus®

# Thank You

---

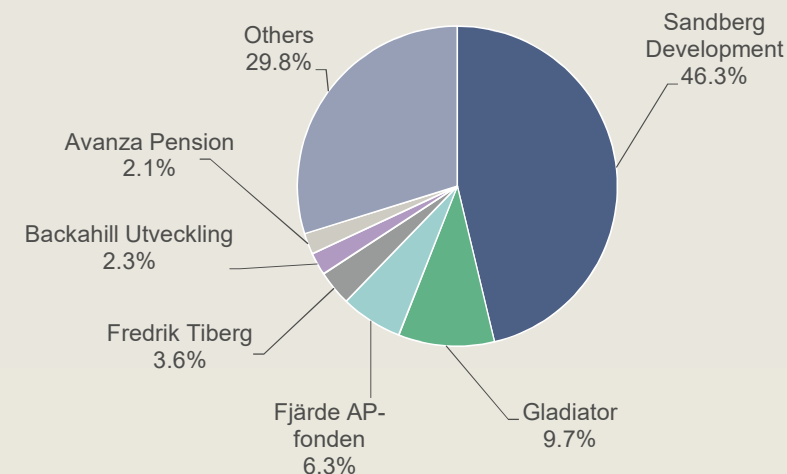
Camurus AB, Ideon Science Park, SE-223 70 Lund, Sweden  
info@camurus.com [camurus.com](https://www.camurus.com)

## Financial overview

MSEK	Q1 2019	Q1 2018
Net revenue	18.5	14.6
- product sales	11.0	3.0
Operating result	-84.4	-46.4
Result after tax	-76.6	-36.3
Cash position	406.6	266.6

Rights issue with gross proceeds of SEK 403 million completed in March 2019

### Key Shareholders (31 March 2019)



**Listed on Nasdaq STO (ticker CAMX)**

**Market Cap:** SEK ~3.4 billion (USD ~360 million)

**Cash position:** SEK ~407 million (31 Mar 2019)

**Employees:** 110

**HQ:** Lund, Sweden

**Regional offices:** Cambridge, Mannheim, Paris, Sydney

## EU ABBREVIATED PRESCRIBING INFORMATION

### Buvidal® (buprenorphine) prolonged-release solution for injection

Please refer to the Summary of Product Characteristics (SmPC) before prescribing.

**Presentations:** Prolonged-release solution for injection in pre-filled syringes containing buprenorphine for weekly injection (8 mg, 16 mg, 24 mg, 32 mg) or monthly injection (64 mg, 96 mg, 128 mg).

**Indication:** Treatment of opioid dependence within a framework of medical, social and psychological treatment. Treatment is intended for use in adults and adolescents aged 16 years or over.

**Dosage and Administration:** Administration of Buvidal® is restricted to healthcare professionals. Appropriate precautions, such as to conduct patient follow-up visits with clinical monitoring to the patient's needs, should be taken when prescribing and dispensing buprenorphine. Take-home use or self-administration of the product by patients is not allowed. *Precautions to be taken before initiation of treatment:* To avoid precipitating symptoms of withdrawal, treatment with Buvidal® should be started when objective and clear signs of mild to moderate withdrawal are evident. For patients using heroin or short-acting opioids, the initial dose of Buvidal® must not be administered until at least 6 hours after the patient last used opioids. For patients receiving methadone, the methadone dose should be reduced to a maximum of 30 mg/day before starting treatment with Buvidal® which should not be administered until at least 24 hours after the patient last received a methadone dose. Buvidal® may trigger withdrawal symptoms in methadone-dependent patients. *Initiation of treatment in patients not already receiving buprenorphine:* Patients not previously exposed to buprenorphine should receive a sublingual buprenorphine 4 mg dose and be observed for an hour before the first administration of weekly Buvidal® to confirm tolerability to buprenorphine. The recommended starting dose of Buvidal® is 16 mg, with one or two additional 8 mg doses at least 1 day apart, to a target dose of 24 mg or 32 mg during the first treatment week. The recommended dose for the second treatment week is the total dose administered during the week of initiation. Treatment with monthly Buvidal® can be started after treatment initiation with weekly Buvidal®, in accordance with the dose conversion in Table 2 of the full SmPC and once patients have been stabilised on weekly treatment (four weeks or more, where practical). *Switching from sublingual buprenorphine products to Buvidal®:* Patients treated with sublingual buprenorphine may be switched directly to weekly or monthly Buvidal®, starting on the day after the last daily buprenorphine sublingual treatment dose in accordance with the dosing recommendations in the full SmPC. *Maintenance treatment and dose adjustments:* Buvidal® can be administered weekly or monthly. Doses may be increased or decreased and patients can be switched between weekly and monthly products according to individual patient's needs and treating physician's clinical judgement as per recommendations in the full SmPC. Following switching, patients may need closer monitoring. Assessment of long-term treatment is based on 48-week data. *Supplemental dosing:* A maximum of one supplemental Buvidal® 8 mg dose may be administered at an unscheduled visit between regular weekly and monthly doses, based on individual patient's temporary needs. The maximum dose per week for patients who are on weekly Buvidal® treatment is 32 mg with an additional 8 mg dose. The maximum dose per month for patients who are on monthly Buvidal® treatment is 128 mg with an additional 8 mg dose. *Missed doses:* To avoid missed doses, the weekly dose may be administered up to 2 days before or after the weekly time point, and the monthly dose may be administered up to 1 week before or after the monthly time point. If a dose is missed, the next dose should be administered as soon as practically possible. *Termination of treatment:* If Buvidal® treatment is discontinued, its prolonged-release characteristics and any withdrawal symptoms experienced by the patient must be considered. If the patient is switched to treatment with sublingual buprenorphine, this should be done one week after the last weekly dose or one month after the last monthly dose of Buvidal® according to the recommendations in the full SmPC.

**Method of administration:** Buvidal® is intended for subcutaneous administration only. It should be injected slowly and completely into the subcutaneous tissue of different areas (buttock, thigh, abdomen, or upper arm), provided there is enough subcutaneous tissue. Each area can have multiple injection sites. A minimum of 8 weeks should be left before re-injecting a previously used injection site with the weekly dose.

**Contraindications:** Hypersensitivity to the active substance or to any of the excipients. Severe respiratory insufficiency. Severe hepatic impairment. Acute alcoholism or *delirium tremens*.

**Special warnings and precautions for use:** Care must be taken to avoid inadvertent injection of Buvidal®. The dose must not be administered intravascularly (intravenously), intramuscularly or intradermally. Intravascular such as intravenous injection would present a risk of serious harm as Buvidal forms a solid mass upon contact with body fluids, which potentially could cause blood vessel injury, occlusion, or thromboembolic events. To minimise the risk of misuse, abuse or diversion, appropriate precautions should be taken when prescribing and dispensing buprenorphine. Healthcare professionals should administer Buvidal directly to the patient. Take-home use or self-administration of the product by patients is not allowed. Any attempts to remove the depot should be monitored throughout treatment. The prolonged-release properties of the product should be considered during treatment including initiation and termination. In particular, patients with concomitant medicinal products and/or co-morbidities, should be monitored for signs and symptoms of toxicity, overdose or withdrawal caused by increased or decreased levels of buprenorphine. Buprenorphine should be used with care in patients with respiratory insufficiency. Buprenorphine may cause drowsiness particularly when taken together with alcohol or central nervous system depressants such as benzodiazepines, tranquilisers, sedatives, gabapentinoids or hypnotics. Buprenorphine is a partial agonist at the mu-opiate receptor and chronic administration can produce opioid dependence. Baseline liver function tests and documentation of viral hepatitis status are recommended prior to starting therapy. Buprenorphine products have caused precipitated withdrawal symptoms in opioid-dependent patients when administered before the agonist effects resulting from recent opioid use or misuse have subsided. Buprenorphine should be used with caution in patients with moderate hepatic impairment. Hepatic function should be monitored regularly whilst on treatment. The use of buprenorphine is contraindicated in patients with severe hepatic impairment. Caution is recommended when dosing patients with severe renal impairment. Caution should be exercised when co-administering Buvidal® with other medicinal products that prolong the QT interval and in patients with a history of long QT syndrome or other risk factors for QT prolongation. For management of acute pain during continued use of Buvidal®, a combination of use of opioids with high mu-opioid receptor affinity (e.g. fentanyl), non-opioid analgesics and regional anaesthesia might be necessary. Titration of oral or intravenous short-acting opioid pain medicinal products (immediate-release morphine, oxycodone or fentanyl) to the desired analgesic effect in patients treated with Buvidal® might require higher doses. Patients should be monitored during treatment. *Interactions:* No interaction studies have been performed with Buvidal®. See SmPC for precautions when co-administering buprenorphine with other drugs. *Fertility, pregnancy and lactation:* Buprenorphine should be used during pregnancy only if the potential benefit outweighs the potential risk to the foetus. Towards the end of pregnancy, buprenorphine may induce respiratory depression in the newborn infant even after a short period of administration. Buprenorphine and its metabolites are excreted in human breast milk and Buvidal® should be used with caution during breast-feeding. There are no or limited data on effects of buprenorphine on human fertility. *Driving and operating machines:* Buprenorphine has minor to moderate influence on the ability to drive and use machines when administered to opioid-dependent patients. The patient should be cautioned not to drive or operate hazardous machinery whilst taking this medicine until it is known how the patient is affected by the medicine.

**Undesirable effects:** The adverse reactions most frequently reported for buprenorphine are headache, nausea, hyperhidrosis, insomnia, drug withdrawal syndrome and pain. *Very common (≥ 1/10):* insomnia, headache, nausea, hyperhidrosis, drug withdrawal syndrome, pain. *Injection site reactions:* in the double-blind, phase 3 efficacy trial, injection site-related adverse reactions were observed in 36 (16.9%) of the 213 patients (5% of the administered injections) in the Buvidal® treatment group. The most common adverse reactions were injection site pain (8.9%), injection site pruritus (6.1%) and injection site erythema (4.7%). The injection site reactions were all mild or moderate in severity and most events were transient. See full SmPC for further details of adverse reactions.

**Overdose:** General supportive measures should be instituted, including close monitoring of respiratory and cardiac status of the patient. Symptomatic treatment of respiratory depression, following standard intensive care measures, should be instituted. The long duration of action of buprenorphine and the prolonged release from Buvidal®, should be taken into consideration when determining length of treatment needed to reverse the effects of an overdose.

**Package quantities:** Pack contains 1 pre-filled syringe with stopper, needle, needle shield, safety device and 1 plunger rod. Pre-filled syringes for weekly injection: 8 mg, 16 mg, 24 mg, 32 mg. Pre-filled syringes for monthly injection: 64 mg, 96 mg, 128 mg.

**Marketing authorisation numbers:** EU/1/18/1336/001, EU/1/18/1336/002, EU/1/18/1336/003, EU/1/18/1336/004, EU/1/18/1336/005, EU/1/18/1336/006, EU/1/18/1336/007.

**Legal category:** Prescription medicine. Further information is available from the **Marketing Authorisation Holder:** Camurus AB, Ideon Science Park, SE-223 70 Lund, Sweden. Phone: +800 2577 2577.

**Date of preparation:** December 2018. *Internal approval number (from Veeva): INT-BUV-1800007.*

**Adverse events should be reported according to national guidelines.**