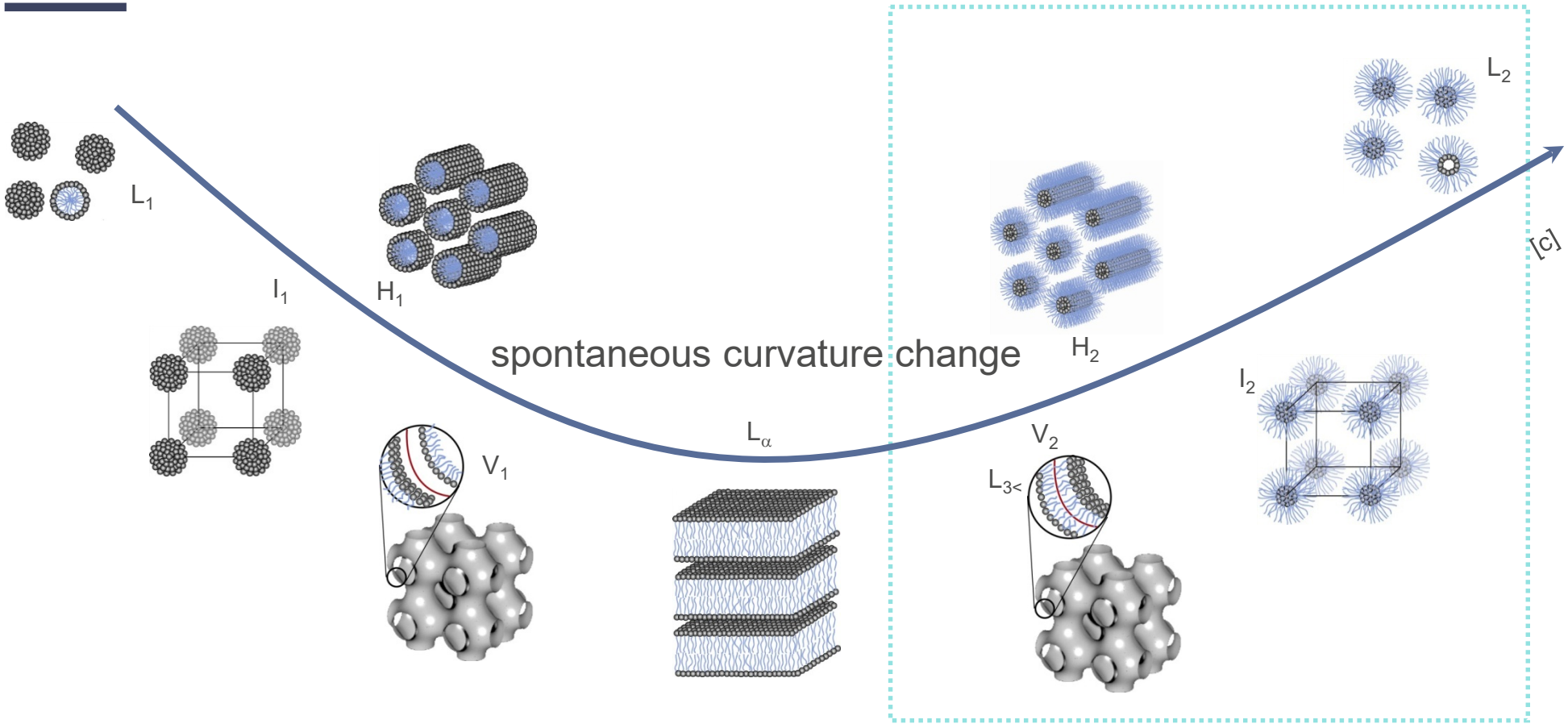
camurus®

FluidCrystal – a new lipid liquid crystal based LAI technology validated by recent product approvals

Dr Fredrik Joabsson
Camurus

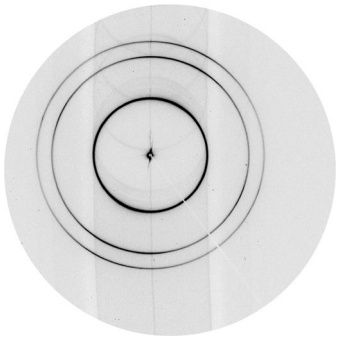
Common self-assembly structures of polar lipids in aqueous media



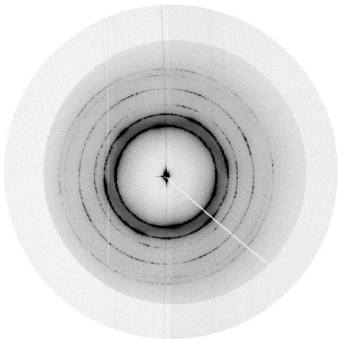
Nanostructure of lyotropic liquid crystalline phases can be determined by X-ray diffraction

Lamellar

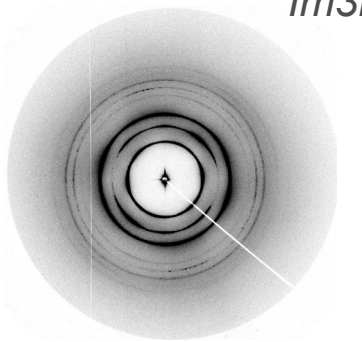
Hexagonal



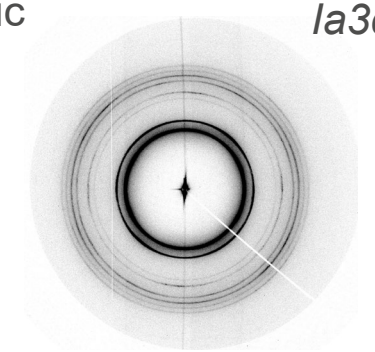
Pn3m cubic



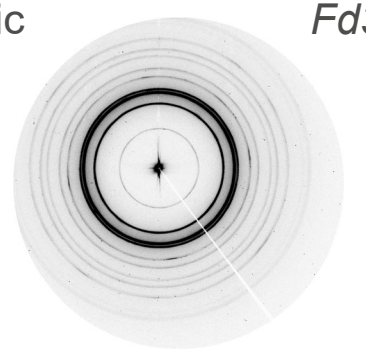
Im3m cubic



Ia3d cubic

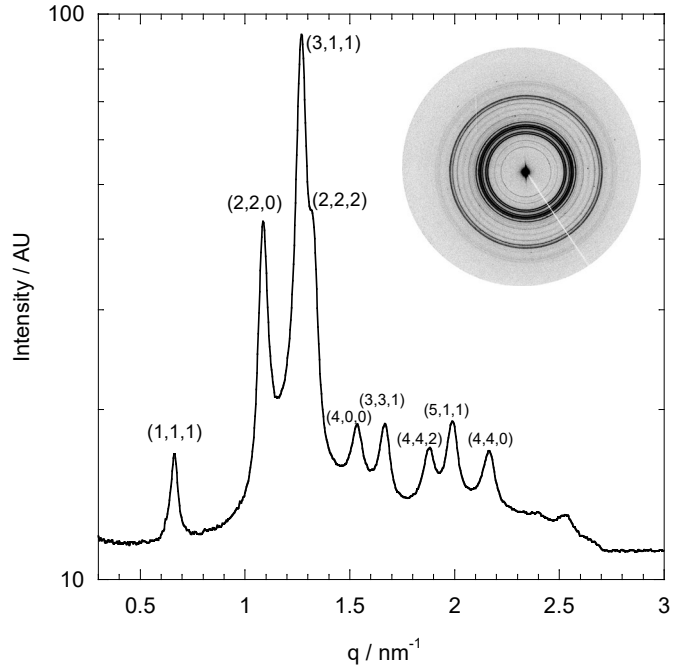


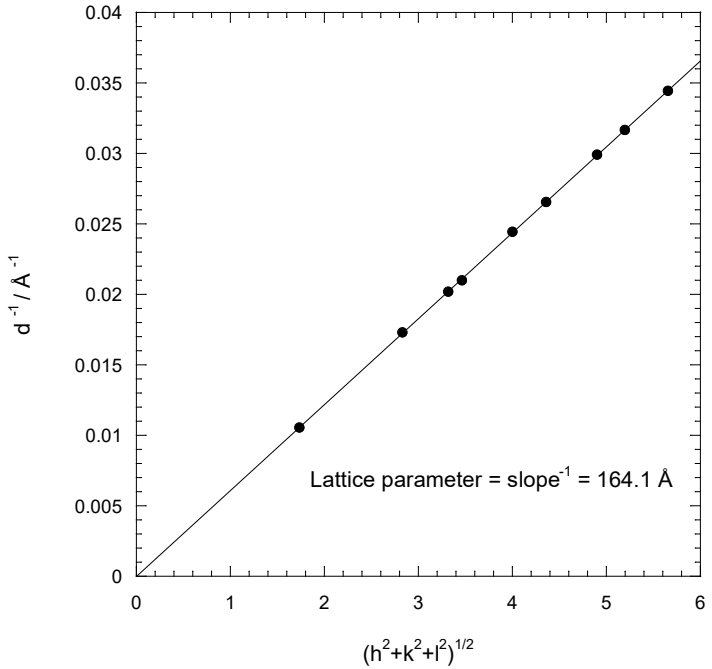
Fd3m micellar cubic



Diffraction pattern translates to structure

Example: Synchrotron X-ray diffraction analysis of a lipid sample along the dilution line passing through the reversed micellar cubic phase (I_2)

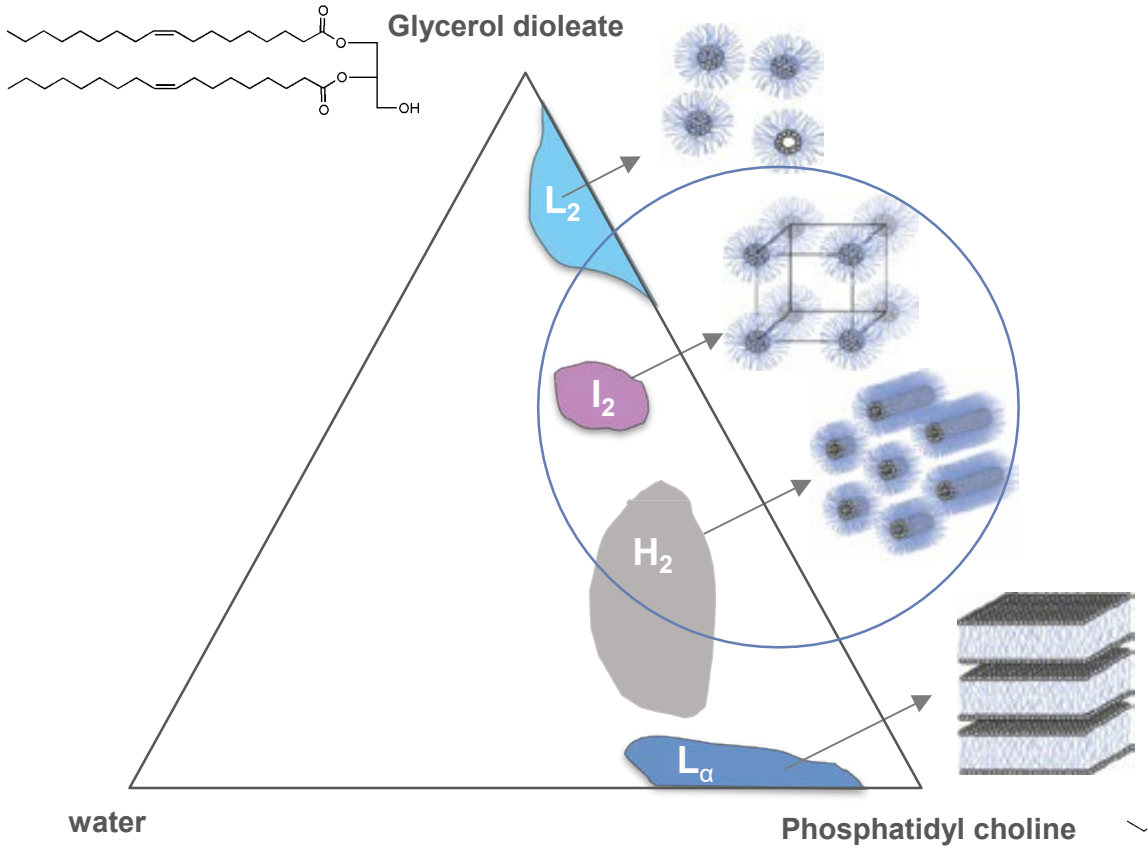




Data consistent with a discontinuous reversed micellar cubic phase with space group *Fd3m*

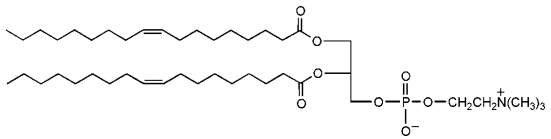
See also *Seddon et al., Phys. Chem. Chem. Phys., 2000, 2, 4485-4493*

FluidCrystal® delivery technology is based on reversed non-lamellar liquid crystalline phases



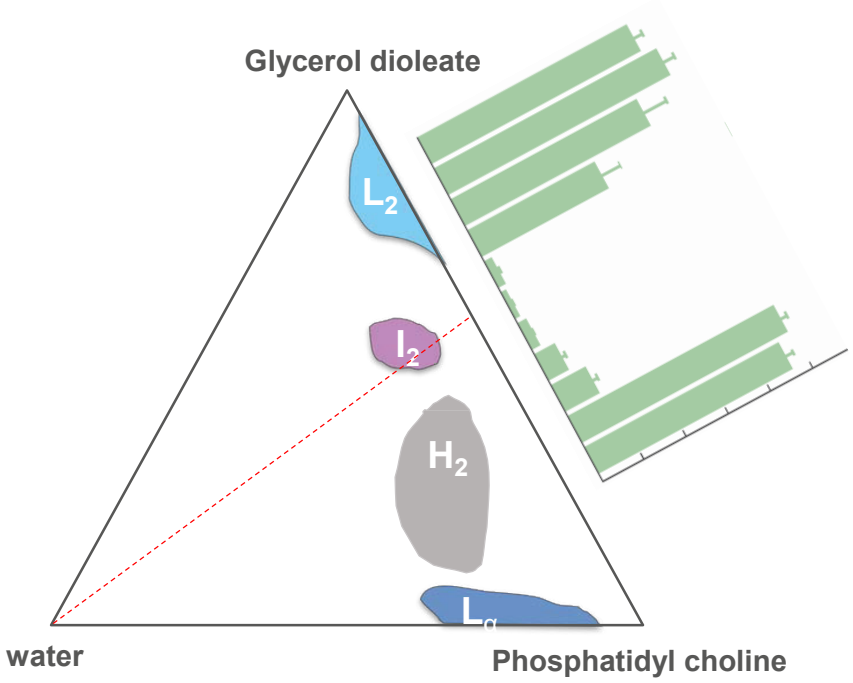
FluidCrystal phase behavior suited for controlled release applications

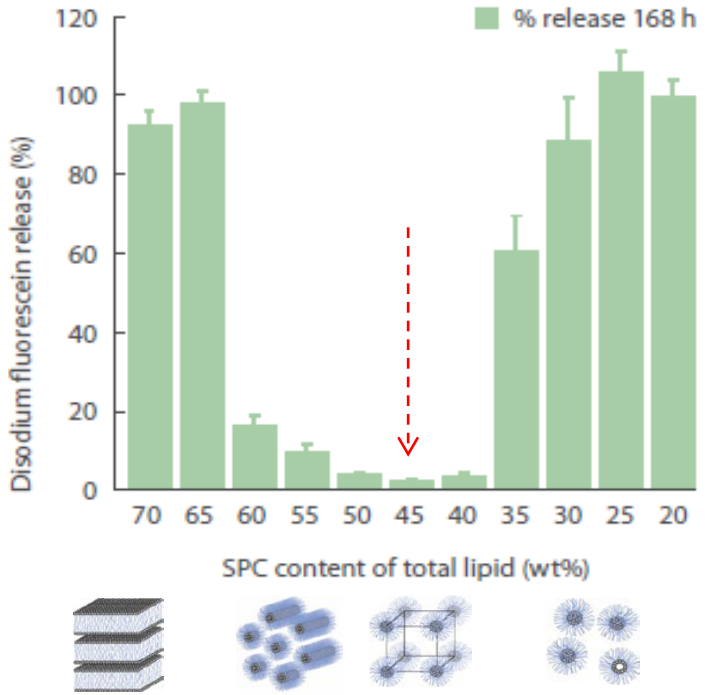
- Oily liquid without the presence of water
  - Easy to handle and prepare
- Forms gel-like liquid crystal phases with discrete domains
  - Effective in entrapping encapsulated compounds
- Stable towards dilution
- Biodegradable lipids with low chemical activity
- Non-ionic lipids
  - Not pH-dependent phase behavior
  - Temperature stable phase behavior



Tuning release by choosing liquid crystal phase

Reversed non-lamellar liquid crystalline phases show very effective encapsulation





Tiberg F, Johnsson M, Nistor C, Joabsson F, in: D. J. Burgess and J. C. Wright (Eds.), Long-Acting Injections and Implants, CRS, Springer, New York, 2012, p. 315.

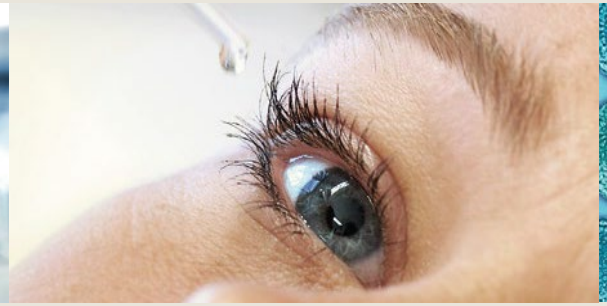
FluidCrystal technology platforms

400+
PATENTS & APPLICATIONS

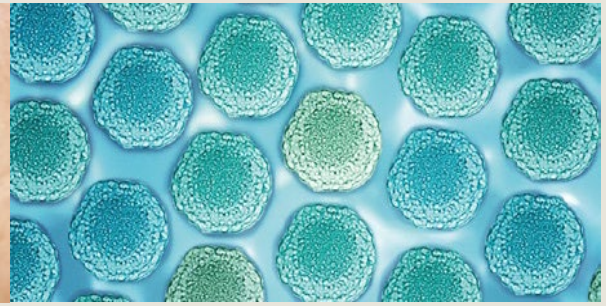
20+
CLINICAL TRIALS WITH FLUIDCRYSTAL® TECHNOLOGY

3
COMMERCIAL PRODUCTS

FluidCrystal® INJECTION DEPOT

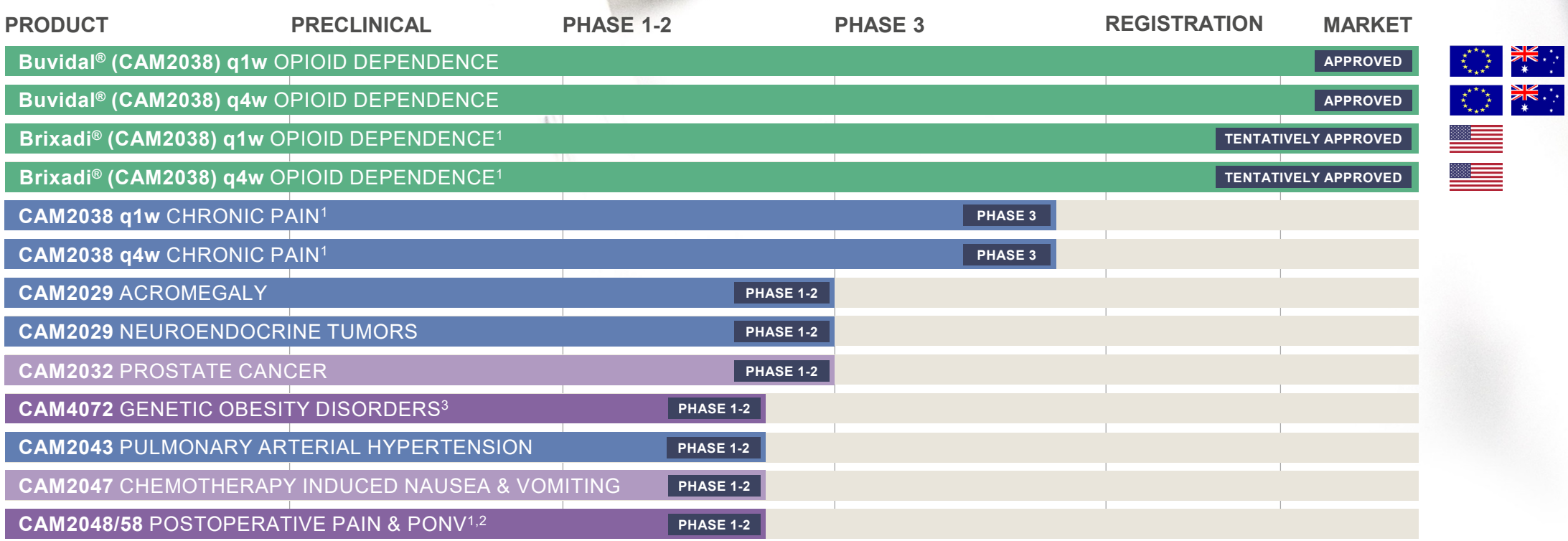


FluidCrystal® TOPICAL BIOADHESIVE



FluidCrystal® NANOPARTICLES

FluidCrystal is the basis for Camurus' broad and diversified product pipeline

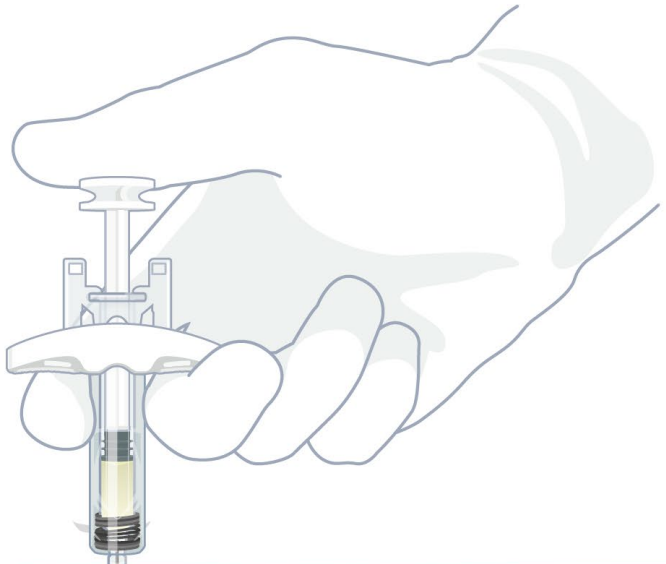


1. Braeburn holds the rights to North America; 2. Postoperative nausea and vomiting; 3. Developed by Rhythm Pharmaceuticals under a worldwide license to FluidCrystal®

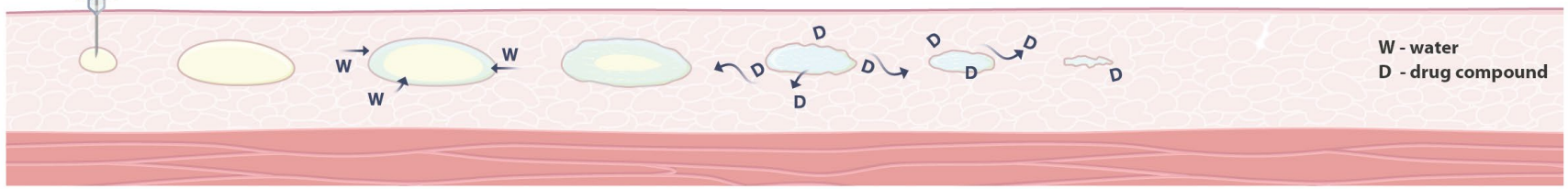
Key technology platform: FluidCrystal injection depot

- First pharmaceutical products based on technology **approved in Nov 2018**.

FluidCrystal injection depot – in situ gel formation



- ✓ Unique patented mixtures of natural lipids
- ✓ Rapid onset & long-acting release
- ✓ Easy to administer
- ✓ Applicable across substance classes
- ✓ Good safety profile
- ✓ Standard manufacturing processes



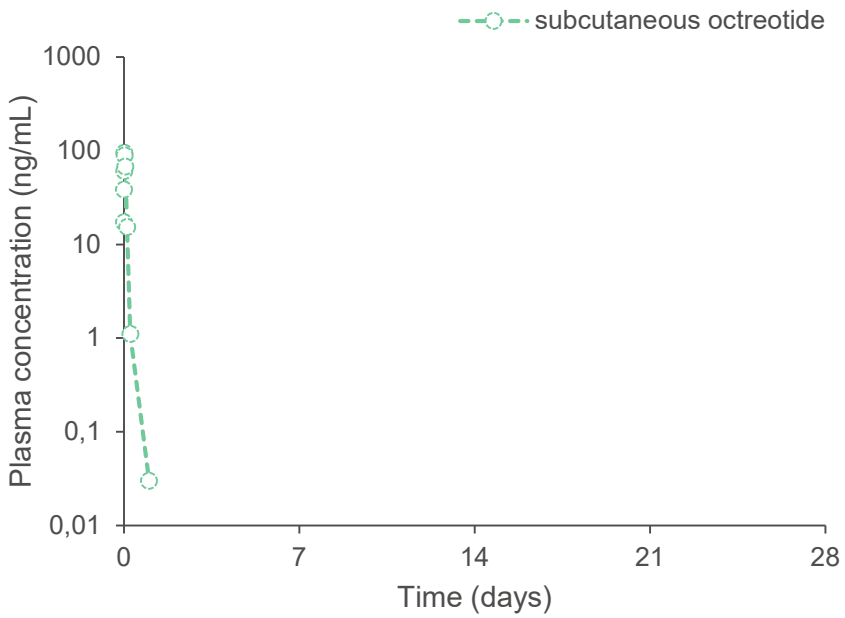
~2000

SUBJECTS HAVE RECEIVED >20,000 INJECTIONS IN CLINICAL TRIALS

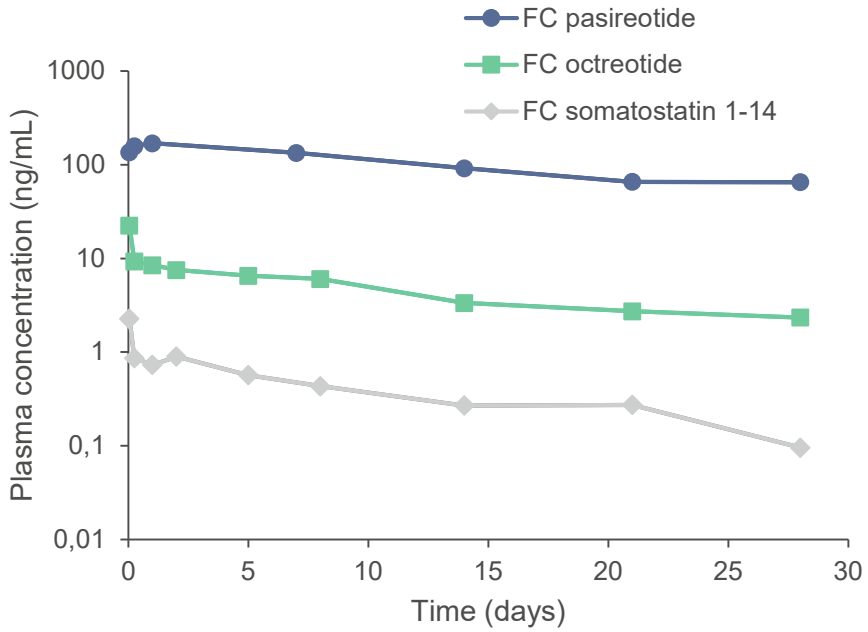
Injection of liquid 〉 Gel formation triggered by water uptake 〉 Slow release of drug 〉 Complete resolution of depot matrix

FluidCrystal – Long-acting peptide release

Immediate release octreotide (Sandostatin®)



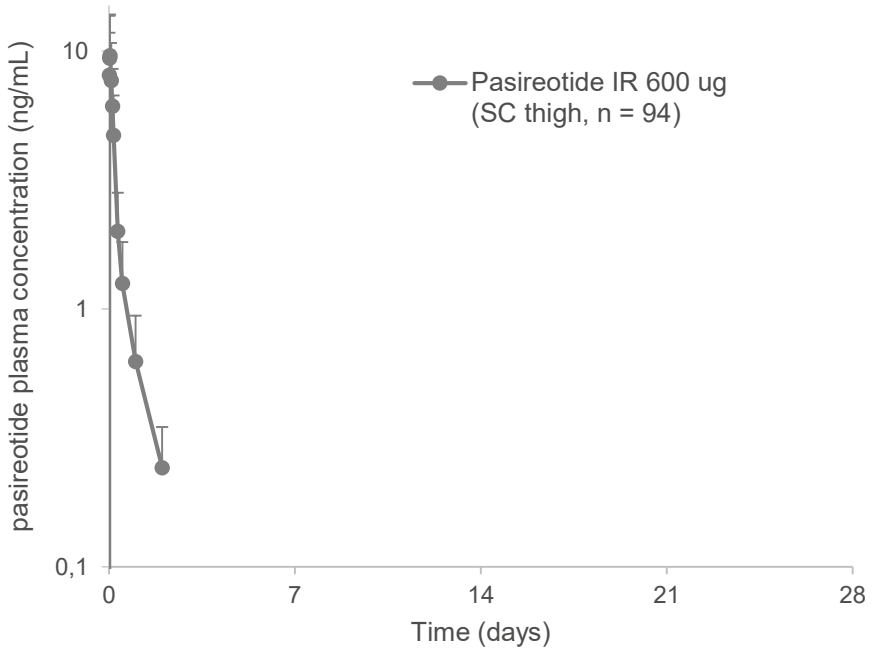
FluidCrystal® injection depot



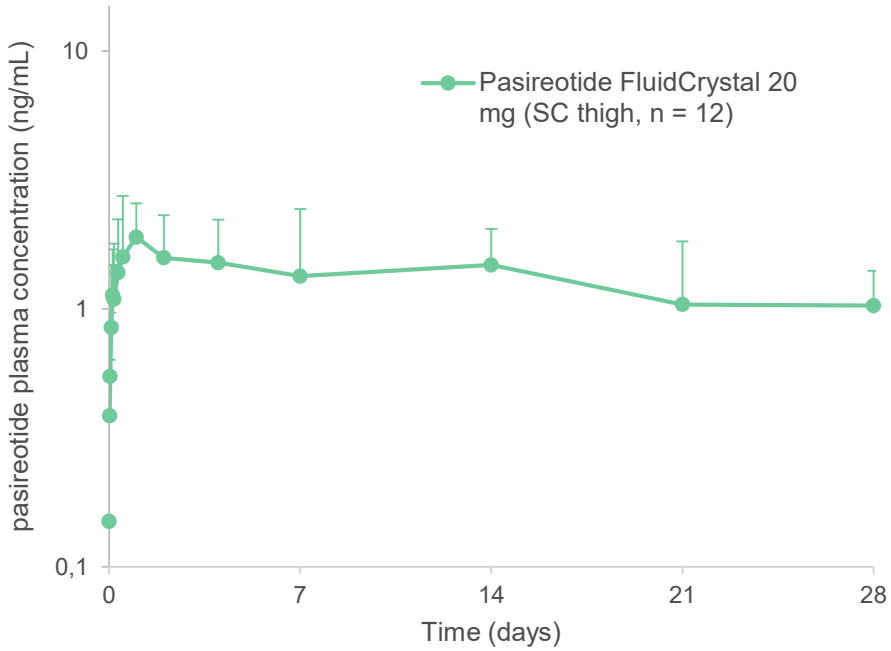
Single dose injection at t=0; n=6 (SC); rodent; mean values

FluidCrystal – Long-acting peptide release

Immediate release pasireotide (Signifor®)



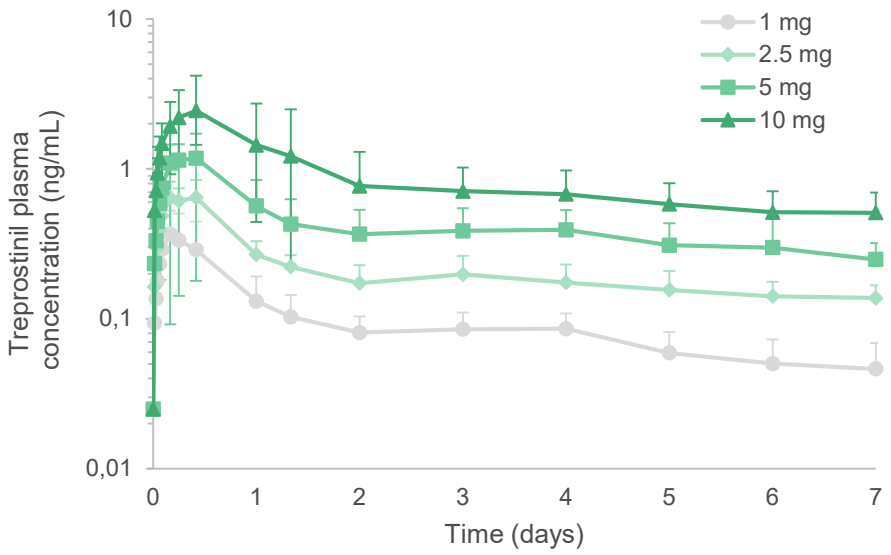
Pasireotide FluidCrystal® (CAM4071)



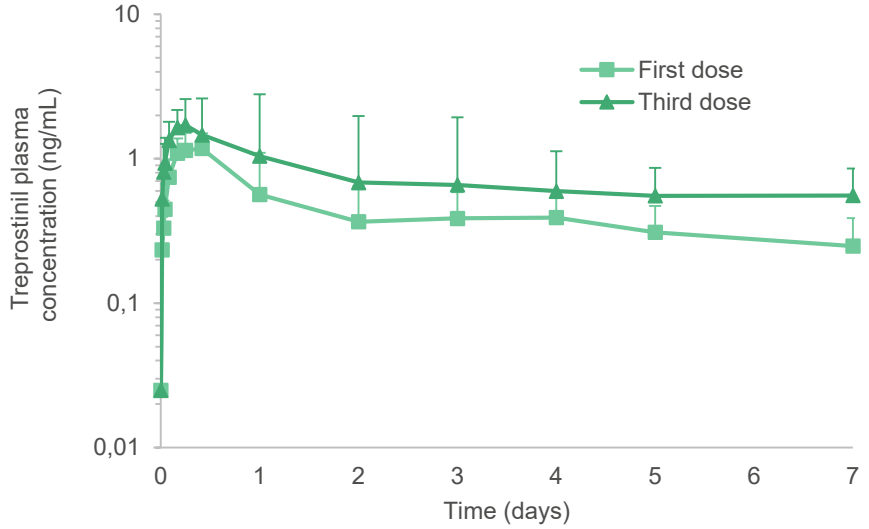
Single dose injection at t=0; clinical Phase 1 data, mean values. Tiberg, F. et al, Poster presentation at ECE, Barcelona, May 2018

FluidCrystal – Long-acting small molecule release

Single dose treprostinil PK profiles



Repeat dose treprostinil PK profile

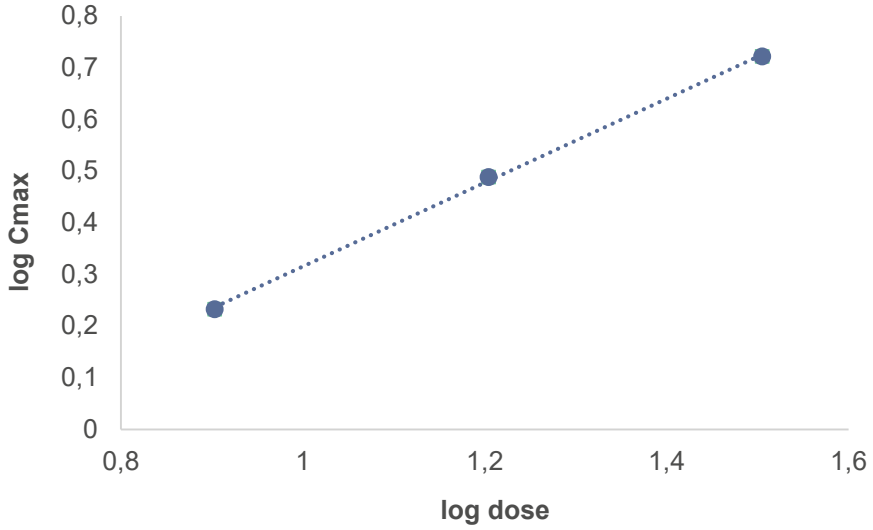


Weekly dosing 5 mg dose

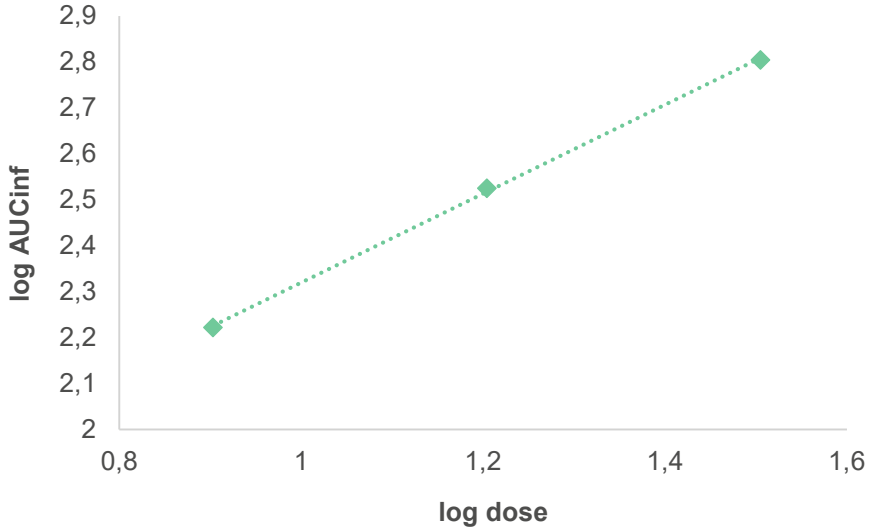
Source: Phase 1 data. Camurus data on file 2018. Maximum dose exposure limited by healthy volunteer study population

Dose adjustment by dose volume

Dose linearity in C_{max}



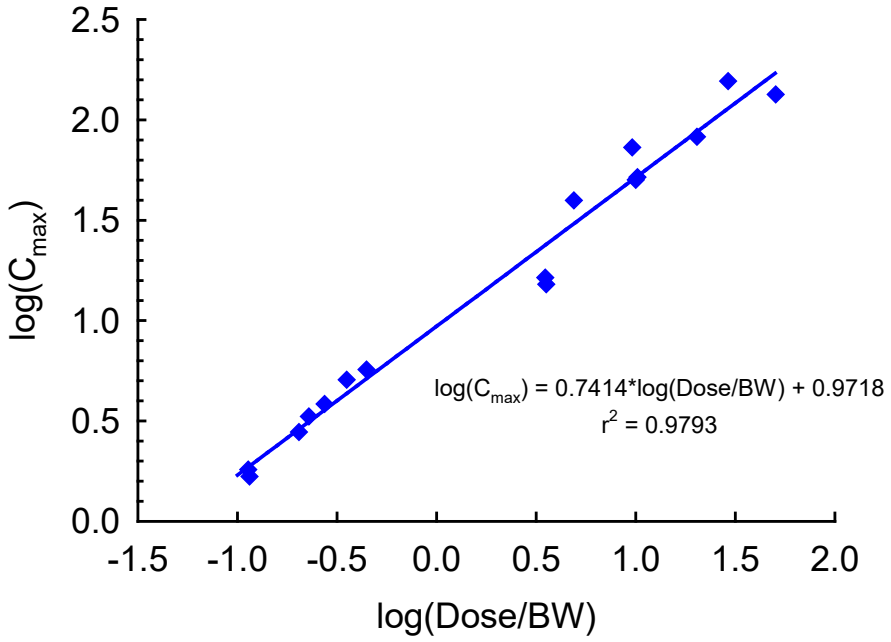
Dose linearity in AUC



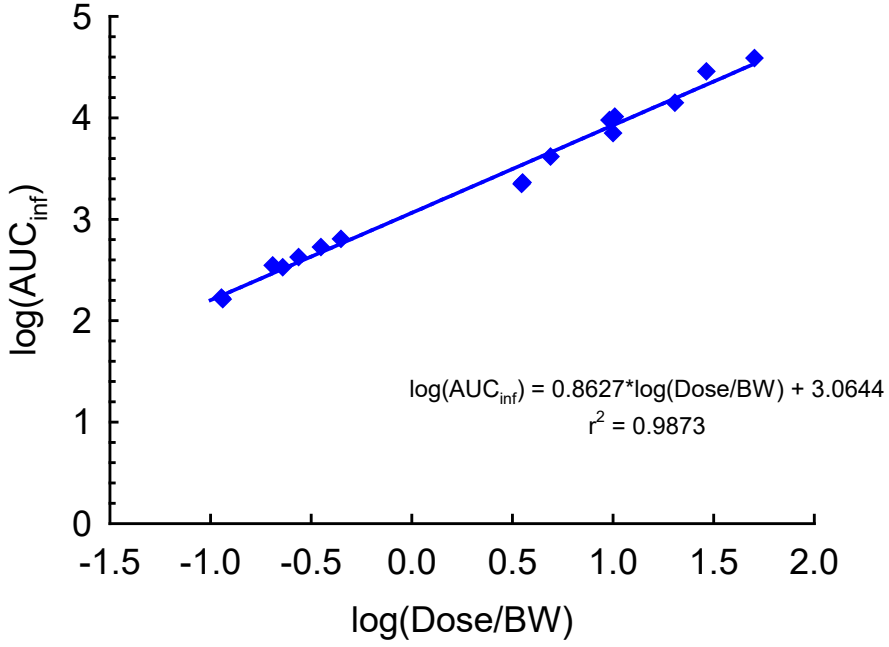
Formulation composition is constant for all doses. Dose adjusted by dose volume (in this case 0.16 – 0.64 mL).
Human data (small molecule in FluidCrystal)

Species correlation

Subcutaneous administration of FluidCrystal small molecule formulation (rat, dog, human)



C_{max} correlation

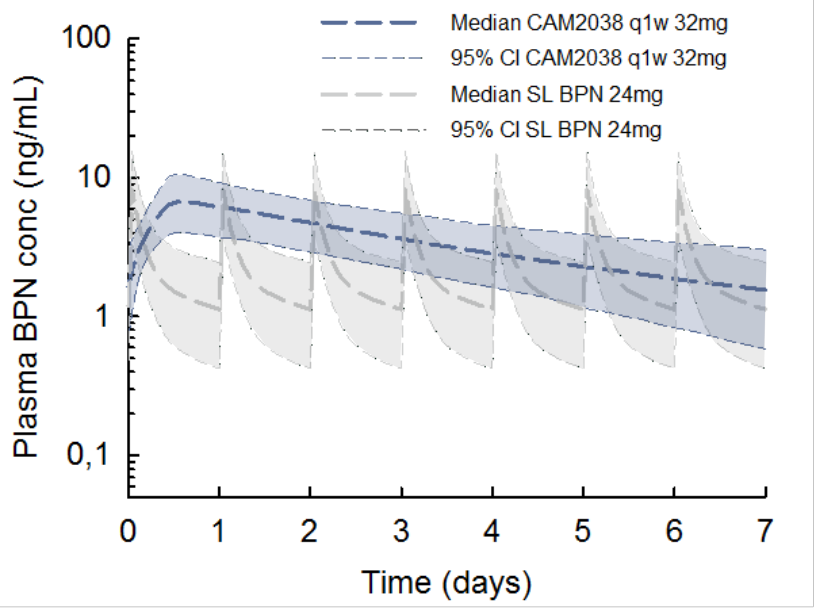


AUC correlation

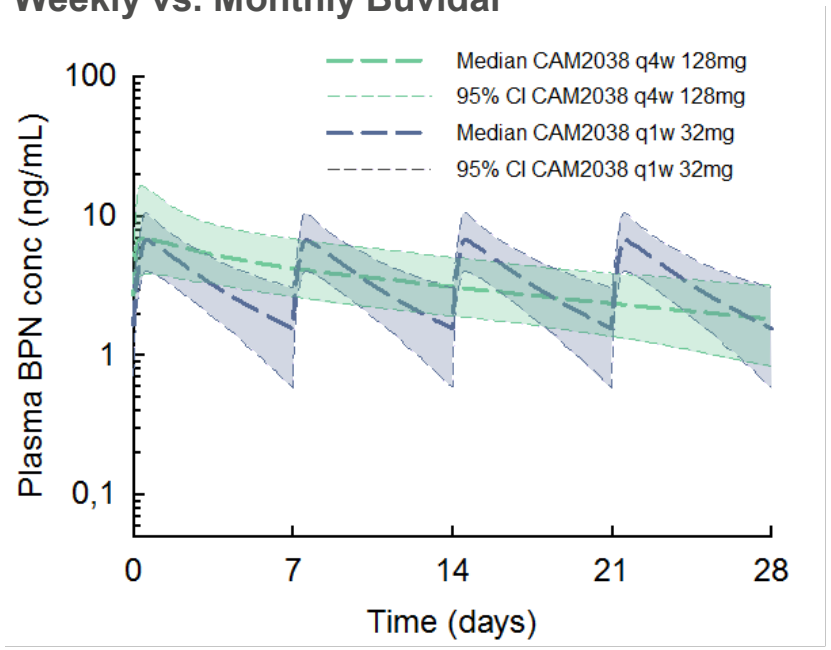
Building the regulatory case: Bridging from daily to weekly or monthly dosing

Illustration of population pharmacokinetic profiles for Buvidal vs sublingual buprenorphine

Weekly Buvidal vs. Daily sublingual buprenorphine



Weekly vs. Monthly Buvidal



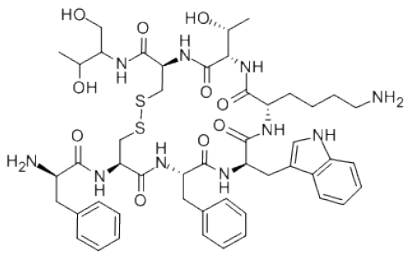
Population PK analysis and modelling based on data from four clinical studies (N=236). Diagnostic testing demonstrated predictive buprenorphine concentrations and good agreement between observed and predicted data percentiles. Steady state data.

Sources: *Abstract presented at the Annual conference of the Society for the Study of Addiction- November 2018; Albayaty M, Linden M, Olsson H, Johnsson M, Strandgarden K, Tiberg F. Adv Ther. 2017;34(2):560–575.*

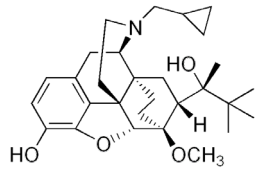
FluidCrystal – Broadly applicable

Broadly applicable across molecular classes

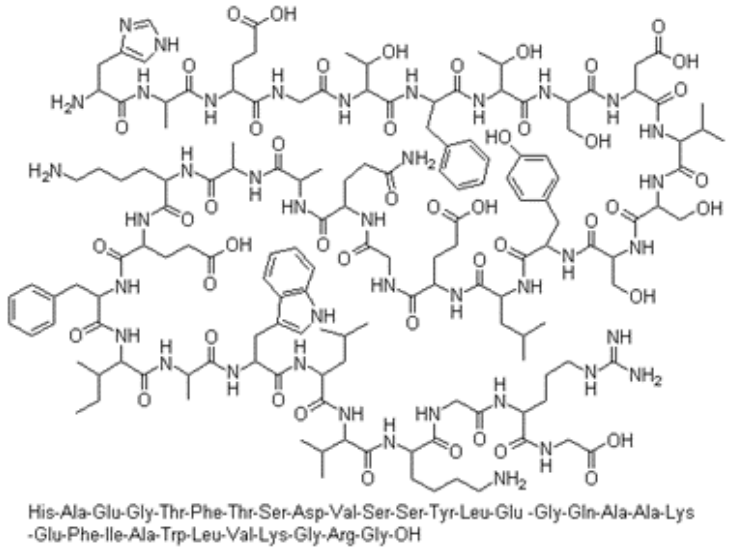
- Peptides & proteins, e.g.:
  - somatostatin & analogues
  - LHRH agonists
  - Glucagon & insulin
  - GLP-1 & analogues
  - MC4 agonists
  - antibody fragments
- Small molecules, e.g.:
  - Opioids
  - local analgesics
  - hormones
  - anti-emetics
  - local antibiotics
  - prostacyclins



Octreotide MW 1019 g/mol



Buprenorphine MW 468 g/mol

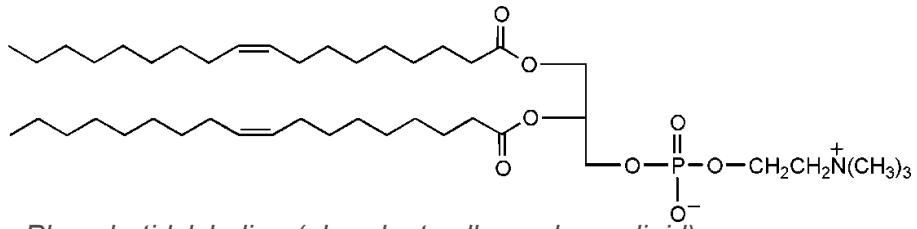


Glucagon-like Peptide 1 MW 3356 g/mol

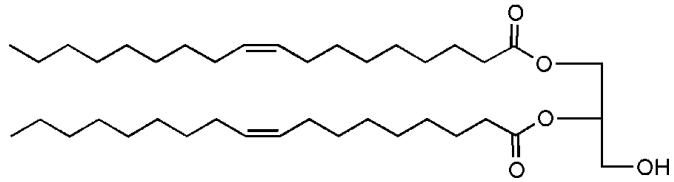
FluidCrystal – Documented safety

FluidCrystal injection depot is a documented safe system

- Natural lipid components (endogenous structures)
- Biocompatible solvents
- Biodegradable liquid crystal matrix
- ~20 clinical trials completed or under completion for FluidCrystal® injection depot
- More than 20,000 injections of FluidCrystal® depot products administered to more than 2,000 human subjects
  - Pharmacokinetic/pharmacodynamic profiles suitable for weekly and monthly dosing
  - Good systemic tolerability and safety profile
  - Good local tolerability



Phosphatidylcholine (abundant cell membrane lipid)



Glycerol dioleate (first metabolite of standard triglyceride such as olive oil)

FluidCrystal – Straight-forward and scalable manufacturing

Manufacturing of FluidCrystal® based products

– Commercially available high quality sources of key components
– Manufacturing using conventional pharmaceutical processing steps
– Straightforward up-scaling

FluidCrystal – Convenient ready-to-use product design

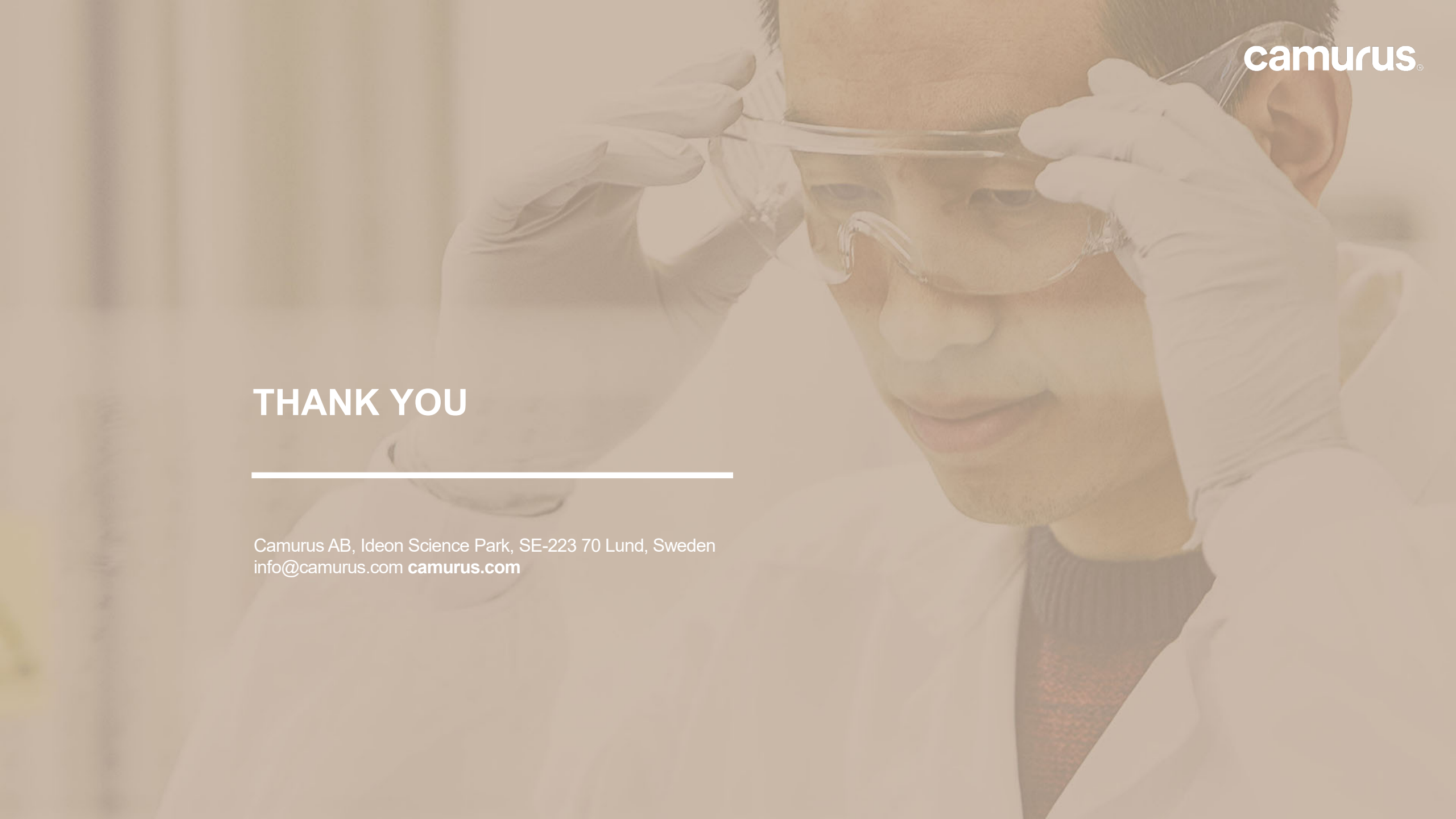
Easy to handle for healthcare professionals or patients

- Compatible with pre-filled syringes
- Compatible with injection aid devices such as autoinjectors
- Enabling patient self-administration
- Room temperature storage
  - Fall-back at refrigerated storage conditions

Active intellectual property strategy supporting FluidCrystal

Active intellectual property strategy

- 35 patent families
- More than 400 approved and/or pending patents
- Solid IP position covering FluidCrystal technology with patent coverage at least until 2025/2027 to 2033 and beyond
- Product-specific patents for own and partnered product
- Global strategy, including coverage in all major markets (US, EU-5, Japan)



THANK YOU

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