



Exxel Pharma Presentation

Advancing a novel therapeutic for
patients with chronic cough

October 2021



Exxel Pharma Introduction

Company

- British Columbia corporation; Headquartered in Denver, Colorado
- Management team offers world-class leadership, expert technological know-how and deep pharma experience
- Preclinical & IND-stage programs with first-in-class, patented therapeutics (NCEs)

URB937 Program

- Novel small molecule therapeutic and mechanism of action for treatment of chronic cough
- IND enabling studies and pre-IND meeting completed; **6 months from first human dosing**
- Chronic cough collaboration with large European pharma company

ARN Program

- Early stage preclinical program with application in diseases of the CNS (anxiety, PTSD, phobias, substance addiction)
- Under exclusive Option to License with a specialty pharma company; **licensing income expected in 2022**

The Problem: Chronic Cough



Chronic cough is defined as cough lasting for longer than 8 weeks

Estimated to affect 5% of US population

Refractory chronic cough affects patients where treatment of underlying conditions such as asthma or GERD is ineffective

- No approved or effective treatments exist: There is an urgent, unmet medical need
- Gabapentin, pregabalin, amitriptyline, and low-dose morphine are used off-label with marginal effects and safety concerns
- In March of 2021, the FDA accepted Merck's application for Gefapixant, which may become the first chronic cough drug
- Global chronic cough market estimated to reach \$11B* by 2027

The Solution: URB937

A peripherally restricted FAAH inhibitor

URB937

- A small molecule therapeutic: Easy to manufacture and patent protected
- Licensed from the laboratory of Professor Daniele Piomelli at UC Irvine
- Supported by >25 scientific publications

Mechanism of Action

- Specifically inhibits the FAAH enzyme with broad application in diseases such as chronic cough, pain, hyperactive bladder and migraine headache
- Peripherally restricted by active exclusion from the brain and central nervous system (CNS)
- Exhibits unexpected efficacy and remarkable safety by being entirely excluded from the CNS
- Novel mechanism of action for cough management

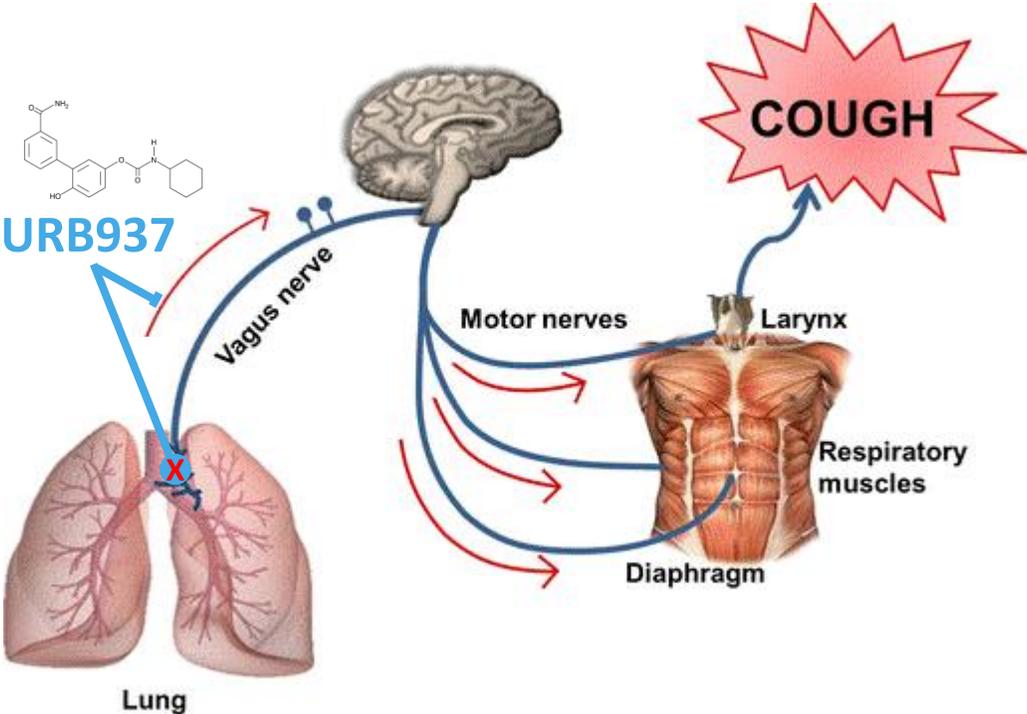
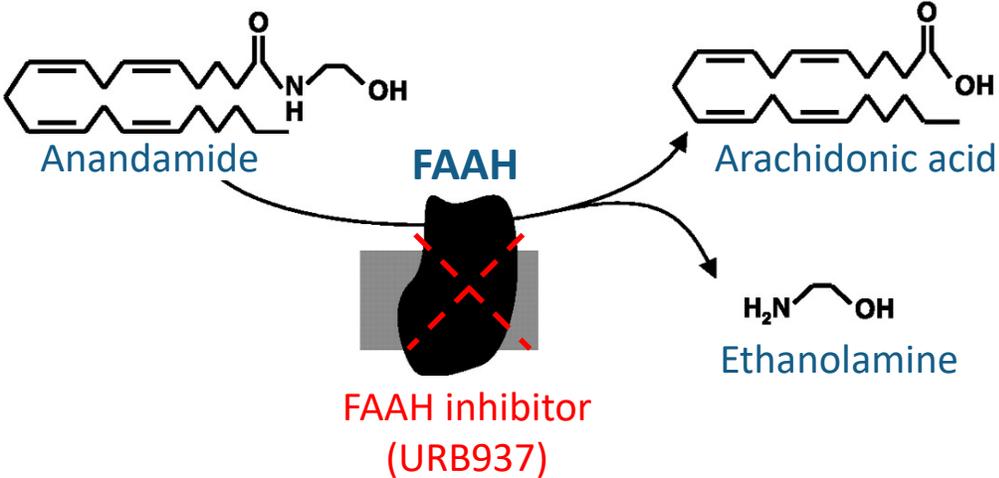
Development Status

- IND enabling studies and pre-IND meeting completed, chance of Fast Track designation
- Preclinical cough collaboration with large European pharma company
- Phase I clinical trial designed and planned with Southern Californian clinical CRO
- Six months away from first human dosing, pending capitalization

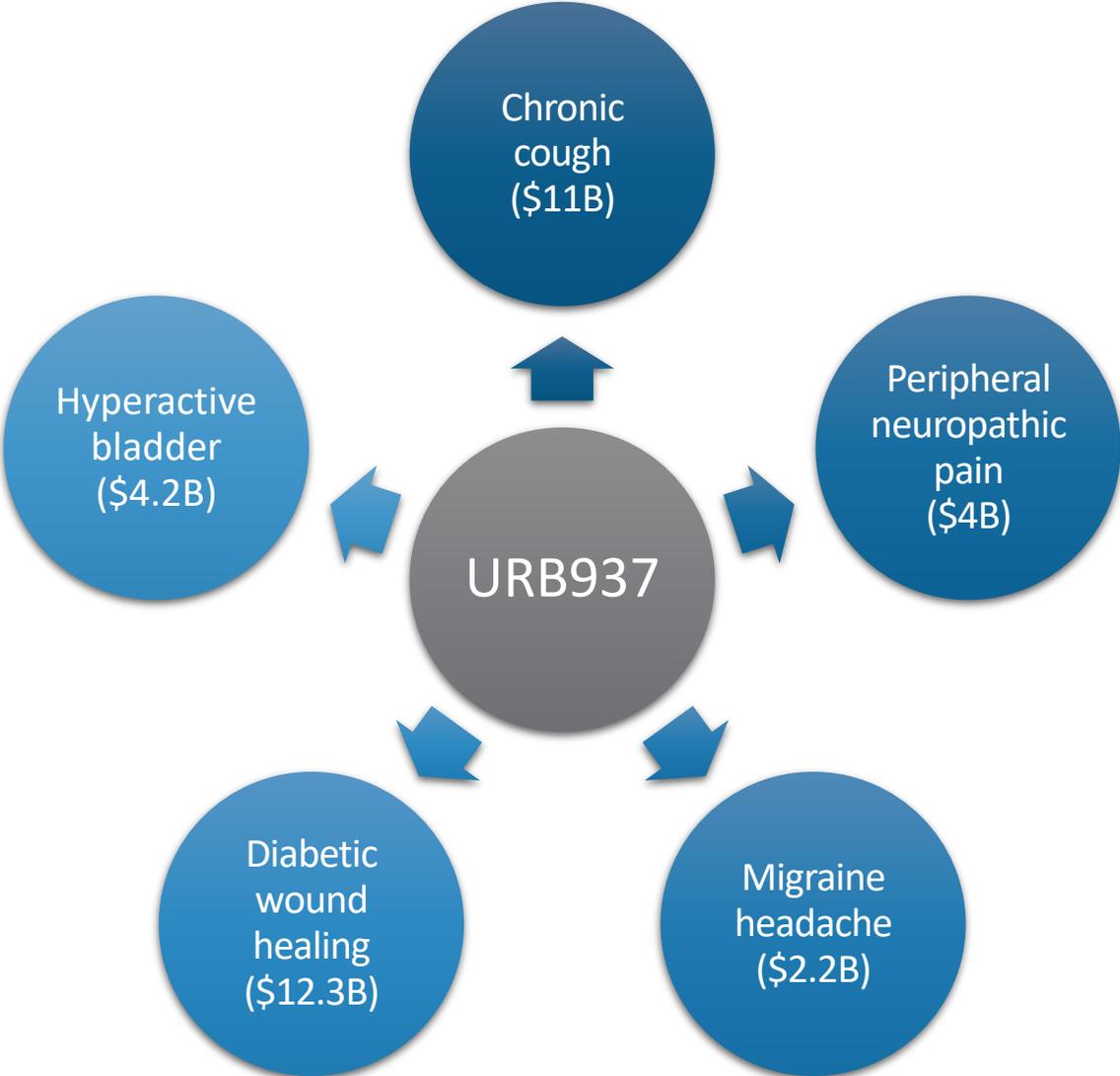


URB937: Mechanism of Action

URB937 boosts the therapeutic effect of naturally occurring Anandamide by preventing its inactivation by FAAH



URB937: A broad range of possible indications



Large global markets may be targeted with URB937

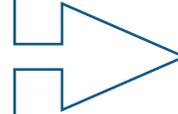
URB937: Program status

IND-enabling safety/pharmacology

- ✓ In vitro drug metabolism
- ✓ GLP Genetox
- ✓ MTD/DRF, rat & dog
- ✓ GLP 28-day tox, rat & dog
- ✓ GLP FOV/Respiratory/CV
- ✓ 10 kg GMP Drug Substance
- ✓ Clean safety profile

Regulatory and clinical development

- ✓ Pre-IND meeting
- ✓ Phase I protocol developed
- ✓ Clinical CRO selected
- ✓ IND and IB drafted
- IND submission pending drug product completion



- Preclinical safety/pharmacology completed
- 6 months from first human dosing (pending capitalization)
- 30 months from human proof of concept (pending capitalization)

ARN Program

Lead indication: PTSD

Status:

- Under an exclusive option to license agreement with a specialty pharma company
 - Molecules in early preclinical development
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ARN program Option & Sublicense terms

In September of 2021, Exxel entered into an exclusive option/license agreement for the early stage ARN program with a private, specialty pharma company.

2022

| | | | | | |
|--------------------|----------------|-----------------|------------------|-------------------------|-------------------------|
| <i>License Fee</i> | <i>Phase I</i> | <i>Phase II</i> | <i>Phase III</i> | <i>First sale in US</i> | <i>First sale in EU</i> |
| <i>\$0.9M</i> | <i>\$1M</i> | <i>\$1M</i> | <i>\$2.5M</i> | <i>\$8M</i> | <i>\$5M</i> |

8.5% royalty on future commercial sales

20-50% of future sublicensing income

Strong near-term income potential with significant long-term royalty and sublicensing income possible

Management Team



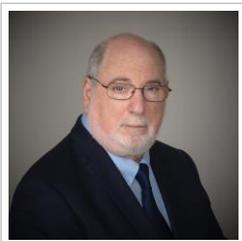
Soren Mogelsvang, PhD
President and CEO, Director

Dr. Mogelsvang is a biotech executive and entrepreneur with 20 years of experience. He is the co-founder of several biotech companies and brings a track record in building and leading privately funded and publicly traded companies. Recent positions he has held include President and CEO of Peak Pharmaceuticals, which he built from concept to a profitable veterinary health company; Co-founder and VP of R&D at Serpin Pharma, a clinical stage biotech company; Co-founder and Head of R&D at Caerus Discovery, an immunology company launched with support from BioWa – Kyowa Hakko Kirin and ImmunoCellular Therapeutics; and Head of Cell Biology at ATCC. Soren has PhD in Cell Biology from the University of Cambridge (UK), an MSc in Plant Molecular Biology from the University of Copenhagen (Denmark), and did postdoctoral research at the University of Colorado School of Medicine.



Daniele Piomelli, PhD, MD (h.c.)
CSO

Daniele is an Italian-born American scientist. He studied neuroscience in New York City, with James H. Schwartz and Eric R. Kandel at Columbia University College of Physicians and Surgeons (PhD, 1983-1988) and later with Paul Greengard at the Rockefeller University (Post-doc, 1988-1990). Two of his mentors (ERK and PG) received the Nobel Prize for their contributions to medicine in 2000. After working at the INSERM in Paris (1990-1995) and at the Neurosciences Institute in La Jolla (1995-1998) with Nobel Laureate Gerald Edelman, he joined the University of California Irvine School of Medicine, where he is now Louise Turner Arnold Chair in Neurosciences and Professor of Anatomy and Neurobiology, Pharmacology and Biological Chemistry. Daniele is scientific cofounder of Kadmus Pharmaceuticals, Thesan Pharmaceuticals and NeoKera.



Richard Paul, MD
CMO

Dr. Paul is a licensed MD with more than two decades of experience in drug development, regulatory affairs and clinical research. His career started with post graduate work at Albert Einstein College of Medicine, Rutgers University's Internal Medicine Residency program and a Fellowship tenure at Harvard Medical School/Joslin Diabetes Center. After 9 years of clinical practice, he transitioning into pharmaceutical research with Pfizer and subsequently held executive leadership positions in clinical research, regulatory and medical safety departments with Ergo Science, Grünenthal USA, Shionogi USA and Schering Plough Corporation. Notably, Dr. Paul was the founding Managing Director of Grünenthal USA, establishing the subsidiary for Grünenthal GmbH of Germany. Rich's experience spans medical safety, clinical research, and regulatory strategy. He has multi-divisional FDA experience having supported a number of Investigational and New Drug Applications with the US FDA and other international regulatory agencies.

Non-Executive Board of Directors



Nitin Kaushal
Director

Mr. Kaushal is a Managing Director in the Deals practice at PwC Canada. Nitin has more than 25 years experience in the financial investing, life sciences, consumer health care, health care services and medical device industries. His experience includes board of directorships with pharmaceutical and health care companies. He has also held senior roles in investment banking, venture capital and consulting firms. Nitin has performed over 50 merger, acquisition, strategic advisory, and licensing assignments. He has been an advisor to many of the leading global pharma companies and has participated in capital market transactions raising in excess of \$2Bn.



Guy Yachin
Director

Mr. Yachin is the CEO and Executive Chairman of Xerient, a drug development company focused on enhancing radiation therapy. Previously, he served as CEO of Serpin Pharma, a Virginia based immunotherapy company. Mr. Yachin is a serial entrepreneur who has served as CEO for numerous biomedical companies. His notable achievements include serving as the CEO of MGVS during collaborative funding with Teva Pharmaceuticals in 2009 and co-founding Chiasma Inc. which entered into a \$600MM licensing agreement with Roche in 2013. He is the former CEO of Naiot Technological Center in Israel where he played an active role in establishing, managing and raising over \$50M for over a dozen biomedical startup companies. As CEO of NasVax Ltd. he successfully led the company's capital acquisition efforts on the public and private markets. Mr. Yachin has sat on the board of multiple companies including Orgenesis, Remon Medical Technologies, Enzymotec and NanoPass. He holds a BSc. and an MBA from Technion – Israel Institute of Technology.



Nancy Retzlaff
Director

Nancy Retzlaff is a seasoned biopharmaceutical executive with over 20 years of experience. She began her career in the pharmaceutical industry with Bayer Healthcare in Canada and has since held commercial leadership positions of increasing responsibility at Bayer US, Schering-Plough and Pfizer. She has also held senior level positions at two start-up biopharma organizations. Nancy brings a track record of leading successful product launches globally as well as in the US, Europe, Japan & Canada, and has led a number of high profile brands including Cipro, Remicade, Lyrica, Aricept and Eliquis. She has broad therapeutic expertise in pain, immunology, neurosciences, infectious diseases and cardiology. Her deep commercial experience spans early commercial development through to life cycle management. Nancy has also served as an advisor to global pharma as well as early start-up companies.

Recent deals in the FAAH and CNS space

2020: Jazz Pharmaceuticals acquired the clinical stage FAAH inhibitor PF-04457845 from SpringWorks for an upfront payment of US\$35M, up to US\$375M in milestone payments and high single-digit royalty on future sales.

2019: Ely Lilly acquired the phase I pain drug CNTX-0290 from Centrexion Therapeutics Corporation. This deal included an upfront payment of US\$47M, up to US\$575M in milestone payments, up to US\$375M in sales milestones and tiered royalty on sales.

2019: Abide Therapeutics, with its phase IIa MGLL inhibitor (boosts endocannabinoid signaling), was acquired by Lundbeck (CPH:LUN) in a deal that had an upfront cash payment of US\$250M plus \$US150M in milestone payments.

2016: Merck acquired Afferent and its cough drug candidate AF-219 (in phase IIb at the time) for US\$500M upfront plus another US\$475M in potential milestone payments. The drug is currently pending FDA review and may become the first approved chronic cough treatment.

Recent deals illustrate the attractiveness of the drug class and indicate the potential value of URB937 as it advances into the clinic

Summary

URB937: First-in-class peripheral FAAH inhibitor

Novel approach to cough and pain management

- MOA backed by peer-reviewed research
- Development supported by non-dilutive grant funding
- Comprehensive patent estate
- IND application and IB drafted
- In-person pre-IND meeting completed
- Strong chance of Fast Track designation
- Clinical protocol developed and CRO selected

Research collaboration with large pharma

ARN: Non-addictive global FAAH inhibitors

Strong licensing potential

- Several pharma companies have indicated interest in the ARN molecules
- Currently under exclusive option to license agreement with a specialty pharma company

Broad application in diseases with significant unmet medical needs

- First clinical proof-of-concept for a global FAAH inhibitor published over the past year
- The early stage ARN compounds are among a few global FAAH inhibitors with meaningful patent life.



Led by an experienced management team

Seeking partners, collaborations and outlicensing opportunities

The background of the slide features a modern building with a glass facade on the right side, reflecting the sky and other buildings. The left side is dominated by a blue gradient with a faint city skyline. A diagonal white line separates the blue gradient from the building image.

For more information

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URB937: Peer-reviewed, scientific publications

Greco R, Demartini C, Zanaboni A, Casini I, Icco R, Reggiani A, Misto A, Piomelli D & Tassorelli C. Characterization of the peripheral FAAH inhibitor, URB937, in animal models of acute and chronic migraine. (2021). *Neurobiol Dis.* Jan;147:105157.

Fotio, Y., Palese, F., Guaman Tipan, P., Ahmed, F. & Piomelli, D. Inhibition of fatty acid amide hydrolase in the CNS prevents and reverses morphine tolerance in male and female mice. *Br. J. Pharmacol.* (2020). doi:10.1111/bph.15031

Charrua, A. et al. Fatty acid amide hydrolase inhibition normalises bladder function and reduces pain through normalising the anandamide/palmitoylethanolamine ratio in the inflamed bladder of rats. *Naunyn Schmiedebergs Arch Pharmacol* 393, 263–272 (2020).

Jiang, H.-X. et al. Inhibition of Fatty Acid Amide Hydrolase Improves Depressive-Like Behaviors Independent of Its Peripheral Antinociceptive Effects in a Rat Model of Neuropathic Pain. *Anesth. Analg.* 129, 587–597 (2019).

Slivicki, R. A., Xu, Z., Mali, S. S. & Hohmann, A. G. Brain permeant and impermeant inhibitors of fatty-acid amide hydrolase suppress the development and maintenance of paclitaxel-induced neuropathic pain without producing tolerance or physical dependence in vivo and synergize with paclitaxel to reduce tumor cell line viability in vitro. *Pharmacol. Res.* 142, 267–282 (2019).

Thompson, J. M. et al. Front and hind paw differential analgesic effects of amitriptyline, gabapentin, ibuprofen, and URB937 on mechanical and cold sensitivity in cisplatin-induced neuropathy. *Mol. Pain* 15, 1744806919874192 (2019).

Vozella, V. et al. Pharmacokinetics, pharmacodynamics and safety studies on URB937, a peripherally restricted fatty acid amide hydrolase inhibitor, in rats. *J. Pharm. Pharmacol.* 71, 1762–1773 (2019).

Yin, H. et al. Posttreatment With the Fatty Acid Amide Hydrolase Inhibitor URB937 Ameliorates One-Lung Ventilation-Induced Lung Injury in a Rabbit Model. *J. Surg. Res.* 239, 83–91 (2019).

Slivicki, R. A. et al. Brain-Permeant and -Impermeant Inhibitors of Fatty Acid Amide Hydrolase Synergize with the Opioid Analgesic Morphine to Suppress Chemotherapy-Induced Neuropathic Nociception Without Enhancing Effects of Morphine on Gastrointestinal Transit. *J. Pharmacol. Exp. Ther.* 367, 551–563 (2018).

González-Rodríguez, S. et al. Synergistic combinations of the dual enkephalinase inhibitor PL265 given orally with various analgesic compounds acting on different targets, in a murine model of cancer-induced bone pain. *Scand. J. Pain* 14, 25–38 (2017).

Li, R. et al. The Fatty Acid Amide Hydrolase Inhibitor URB937 Ameliorates Radiation-Induced Lung Injury in a Mouse Model. *Inflammation* 40, 1254–1263 (2017).

Rock, E. M. et al. Suppression of acute and anticipatory nausea by peripherally restricted fatty acid amide hydrolase inhibitor in animal models: role of PPAR α and CB1 receptors. *Br. J. Pharmacol.* 174, 3837–3847 (2017).

Aizawa, N. et al. URB937, a peripherally restricted inhibitor for fatty acid amide hydrolase, reduces prostaglandin E2-induced bladder overactivity and hyperactivity of bladder mechano-afferent nerve fibres in rats. *BJU Int.* 117, 821–828 (2016).

Greco, R. et al. Effects of peripheral FAAH blockade on NTG-induced hyperalgesia--evaluation of URB937 in an animal model of migraine. *Cephalalgia* 35, 1065–1076 (2015).

Sasso, O. et al. Peripheral FAAH and soluble epoxide hydrolase inhibitors are synergistically antinociceptive. *Pharmacol. Res.* 97, 7–15 (2015).

Aizawa, N. et al. Inhibition of peripheral FAAH depresses activities of bladder mechanosensitive nerve fibers of the rat. *J. Urol.* 192, 956–963 (2014).

Moreno-Sanz, G. et al. Structural determinants of peripheral O-arylcarbamate FAAH inhibitors render them dual substrates for Abcb1 and Abcg2 and restrict their access to the brain. *Pharmacol. Res.* 87, 87–93 (2014).

Guindon, J., Lai, Y., Takacs, S. M., Bradshaw, H. B. & Hohmann, A. G. Alterations in endocannabinoid tone following chemotherapy-induced peripheral neuropathy: effects of endocannabinoid deactivation inhibitors targeting fatty-acid amide hydrolase and monoacylglycerol lipase in comparison to reference analgesics following cisplatin treatment. *Pharmacol. Res.* 67, 94–109 (2013).

Martins, D. F., Mazzardo-Martins, L., Cidral-Filho, F. J., Gadotti, V. M. & Santos, A. R. S. Peripheral and spinal activation of cannabinoid receptors by joint mobilization alleviates postoperative pain in mice. *Neuroscience* 255, 110–121 (2013).

Moreno-Sanz, G. et al. Synthesis and structure-activity relationship studies of O-biphenyl-3-yl carbamates as peripherally restricted fatty acid amide hydrolase inhibitors. *J. Med. Chem.* 56, 5917–5930 (2013).

Moreno-Sanz, G. et al. Pharmacological characterization of the peripheral FAAH inhibitor URB937 in female rodents: interaction with the Abcg2 transporter in the blood-placenta barrier. *Br. J. Pharmacol.* 167, 1620–1628 (2012).

Sasso, O. et al. Peripheral FAAH inhibition causes profound antinociception and protects against indomethacin-induced gastric lesions. *Pharmacol. Res.* 65, 553–563 (2012).

Moreno-Sanz, G. et al. The ABC membrane transporter ABCG2 prevents access of FAAH inhibitor URB937 to the central nervous system. *Pharmacol. Res.* 64, 359–363 (2011).

Clapper, J. R. et al. Anandamide suppresses pain initiation through a peripheral endocannabinoid mechanism. *Nat. Neurosci.* 13, 1265–1270 (2010).