Pain Therapeutics
Day One | Monday 21st May 2018

TRANSLATIONAL APPROACHES

08.30 Registration & Coffee

09.00 Chair’s Opening Remarks
Joseph Stauffer, Chief Medical Officer, Cara Therapeutics

09.10 OPENING KEYNOTE
Choosing targets for novel analgesics: mechanistic versus opportunistic approaches
• Translatability of preclinical evidence is debated in the pain field, but are there exceptions that prove [or disprove] the rule?
• Alternatively, can we take an opportunistic approach and focus on targets with clinical evidence provided by serendipity?
• This presentation will address these questions considering various examples
Jenny Laird, Senior Director, Search and Evaluation, Eli Lilly
Lisa Broad, Senior Research Advisor, Eli Lilly

09.50 Drug discovery approaches in neuropathic pain and migraine
• apples and oranges or lemons and limes?
• Therapeutics target distinct facets of disease pathophysiology in neuropathic pain and migraine
• Shared neurobiological mechanisms in neuropathic pain and migraine
• Limitations to drug development – animal models and/or patient populations
• Harmonizing knowledge gained from neuropathic pain research and development with migraine drug discovery
Gordon Munro, Senior Scientist, Danish Headache Centre

10.30 Morning Coffee

11.00 Dissociation of Responses to Heat and Mechanical Stimuli in a Rodent Model of Rett Syndrome
• Children with Rett syndrome show abnormal cutaneous sensitivity. The precise nature of sensory abnormalities and underlying molecular mechanisms remain largely unknown
• tg mice with methyl-Cpg-binding protein 2 (MeCP2) mutation, characteristic of Rett syndrome, showed hypersensitivity to heat stimuli but hyposensitivity to mechanical stimuli (von Frey)
• This dissociation increased with age
Sigal Melvin, Chief Scientific Officer, MD Biosciences

11.40 Translational opportunities and challenges in chronic pain
• Where are we in our understanding of chronic pain and appropriate cellular targets?
• How to bridge the translational gap from preclinical models to patient selection
• Will personalised medicine provide us with new avenues for mechanistic-based treatments?
• Risk signatures and biomarkers – what are the opportunities and challenges in chronic pain?
Alexander Oksche, Executive Director, Mundipharma Research GmbH & Co.KG

12.20 Panel Discussion: Pain vs Nociception: How appropriate is the use of animal models in pain therapeutics
• Role of animal models in the failure of pain therapeutic development
• How reliable are the surrogate markers for pain in animal models
• What are the alternatives to animal models
• Why do pre-clinical trials still use animal models
Gordon Munro, Senior Scientist, Danish Headache Centre
Jenny Laird, Senior Director, Search and Evaluation, Eli Lilly
Alexander Oksche, Executive Director, Mundipharma Research GmbH & Co.KG

13.00 Networking Lunch

14.00 Abdominoplasty as a Novel Analgesic Model for Acute Soft Tissue Pain
• Abdominoplasty has been validated as an acute pain model with high assay sensitivity
• Subjects undergoing abdominoplasty have a relatively high incidence of opioid-based side effects. From an experimental standpoint, this is a positive because it provides an opportunity to demonstrate putative opioid-sparing properties of novel molecules
• There are several key design characteristics that are critical to the success of the model (intraoperative analgesia, specifics of the surgical procedure, provision of rescue drugs)
• The model has certain weaknesses that must be understood when designing clinical programs
Neil Singla, Founder and Chief Scientific Officer, Lotus Clinical Research

14.40 CR845: A novel kappa opioid receptor agonist for acute post-operative pain, chronic pain of osteoarthritis and pruritus
• Discussion of unique pharmacology of CR845
• Analysis of respiratory safety and abuse liability when used for treatment of pain
• Summary of up to date results from phase II osteoarthritis trials
• Future hopes for CR845
Joseph Stauffer, Chief Medical Officer, Cara Therapeutics

15.20 CNTX-4970 a novel CCR2 antagonist with a unique analgesic signature
• Mechanism of action
• Unique analgesic signature in preclinical models
• Using Big Data to identify clinical development targets
• Findings from Phase 1 clinical studies and next steps
Randall Stevens, Chief Medical Officer, Centrexion Therapeutics Corp

16.00 Afternoon Tea

16.30 VM202, a DNA-based Potential Disease-Modifying Treatment for Painful Diabetic Neuropathy
• VM202 is a naked plasmid DNA vector engineered to express two isoforms of human hepatocyte growth factor (HGF)
• In an ongoing Phase 3 clinical study, VM202 (8 mg/leg) or Placebo is administered I.m. to the calf muscle of each leg in a defined multi-injection pattern on Days 0 and 14 and again on Days 90 and 104
• Phase I/II and separate Phase 2 results show robust reductions in foot pain (<0.05 vs. baseline) and a trend in improved sensory function through 9-12 months after initial treatment in subjects receiving VM202
• Pain relieving effects were more pronounced in patients who are not taking Lyrica (pregabalin) and/or Neurontin (gabapentin)
• VM202 demonstrated an excellent safety profile in Phase I/II and Phase 2 clinical studies
William Schmidt, Vice President, Clinical Development, ViroMed

17.10 Zirrelta: Development of an extended release intra-articular therapeutic for osteoarthritis
• Zirrelta microsphere technology – how does it work?
• The challenges of developing an extended release product
• Summary of pre-clinical data
• Summary of clinical studies
• Case study examples
Toni Williamson, Senior Director Non-Clinical Research, Flexion Therapeutics

17.50 Trial conduct in chronic pain conditions: Pitfalls and challenges
• Patient reported outcomes in clinical trials in pain
• Reducing placebo responses
• Patient recruitment challenges
• Data handling and management
• Other considerations
Yanina Flossbach, Associate Medical Director, Novartis

18.30 Chair’s closing remarks and close of day one

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Pain Therapeutics
Day Two | Tuesday 22nd May 2018

08.30 Registration & Coffee

09.00 Co-Chairs’ Opening Remarks
Randall Stevens, Chief Medical Officer, Centrexion
Kerrie Brady, Chief Business Officer, Executive VP Corporate Strategy, Centrexion

TARGETING ION CHANNELS

09.10 The TREK 1 agonists, a promising way to solve the opioid crisis?
• An example of TREK 1 agonists: the substituted acrylic acid derivatives
• In vitro and in vivo pharmacological profile
• Challenges and promises for the future
Jean Deregnaucourt, Scientific Director, INNOPAIN

09.50 CASE STUDY
Development of NMDA receptor modulators in central pain disorders
• The NMDA receptor is an attractive therapeutic target for neuropathic and chronic pain disorders
• The preclinical development, data and pharmacology of NYX-2925 will be presented
• The clinical development strategy for NYX-2925 will be discussed
Torsten Madsen, Chief Medical Officer, Aptinyx

10.30 Morning Coffee

11.00 Selective TARP-dependent AMPA Receptor Antagonists as a Novel Therapy for Chronic Pain
• The role of AMPA receptors in synaptic plasticity in pain pathways
• Expression and functional consequences of Transmembrane AMPA receptor Regulatory Proteins (TARPs)
• Identification of TARP-dependent AMPA receptor antagonists
• Evidence for LY3130481 (CERC-611) as a novel analgesic
Eric Nisenbaum, Group Leader, Neurophysiology, Eli Lilly

11.40 CASE STUDY
Drugging the un-druggable: P2X4 mAbs as therapeutics for pain
• Novel approaches to discovery of antibodies to P2X4
• Functional and electrophysiological characterisation
• Reaching the CNS – application of novel BBB technologies to access the spinal cord with antibody therapies
• Efficacy in preclinical models and next steps
Iain Chessell, VP & Head, IMED Neuroscience, AstraZeneca

12.20 ROUND TABLE DISCUSSION SESSIONS
Depression and chronic pain
• Does constant pain cause depression or is depression a co-symptom of pain caused by intrinsic changes to neurons?
Iain Chessell, AstraZeneca
• Opioid drugs – Amid an opioid crisis, do abuse resistant drugs work and are we doing enough to reduce harm from opioids?
Joseph Stauffer, Cara Therapeutics
• What can the pain therapeutics industry expect with the ageing population?
Randall Stevens, Centrexion
• How should patient engagement be managed clinical trials for analgesic drugs to reduce the placebo effect and increase the success of clinical trials?
Kerrie Brady, Centrexion
• Why are novel analgesic targets so challenging to find and target effectively with drugs?
Jenny Laid, Eli Lilly
• Can stem cells ever replace animal models in preclinical studies? – Benefits and challenges.
Theo Meert, J&J
• Emerging therapies to treat migraine pain – what’s next after CGRP?
Daniel Mikol, Amgen

13.00 Networking Lunch

CURRENT INDUSTRY OUTLOOK

14.00 Big Data for Big Decisions
• How to best develop a portfolio of novel non-opioid products for pain
• Integration of human expertise and artificial intelligence
• Using metadata to qualify big data output
• Can Big Data increase technical success for novel pain drug development?
Kerrie Brady, Chief Business Officer, Executive VP Corporate Strategy, Centrexion

14.40 CASE STUDY
Development update on Erenumab
• The calcitonin gene-related peptide (CGRP) pathway is pathophysiologically relevant in migraine
• Erenumab is an investigational monoclonal antibody targeting the canonical receptor for CGRP
• In episodic migraine prevention studies, erenumab has demonstrated efficacy in reducing migraine frequency and use of acute headache medications
• In chronic migraine, erenumab has demonstrated efficacy in reducing migraine frequency and use of acute medications in patients with or without acute medication overuse
Daniel Mikol, Executive Medical Director, Global Neuroscience Development, Amgen

15.20 Afternoon Tea

15.50 New approaches to developing pain products
• Search for proof of concept testing
• Search for alternative development plans
• New marketing/entry strategies needed
Theo Meert, Head of Global Government Grant Office, Janssen Pharmaceutical NV, J&J

16.30 CASE STUDY
NKTR-181- a novel approach to an old-school target
• Abuse liability of drugs is strongly related to their CNS pharmacokinetics
• NKTR-181 is a first-in-class opioid analgesic with strategic brain entry kinetics
• Limiting the rate of entry of mu-opioid agonists reduces their likeability
• NKTR-181’s inherent long circulating half-life reduces withdrawal symptoms
• Pivotal efficacy, safety, and abuse liability studies are completed
Stephen Dobrestein, Senior Vice President, Research and Development and Chief R&D Officer, Nektar Therapeutics

17.10 An industry perspective from Grunenthal
• Approaching pain as a disease – not just a symptom
• Mapping the landscape of pain
• Using a target-to-disease approach to identify novel compounds for development
Mark Field, Senior Vice President, Head of Global Clinical Development, Grunenthal GmbH

17.50 Updates on the Therapeutic Application of Botulinum Neurotoxin in Pain: A pre-clinical approach
• While the therapeutic application of botulinum neurotoxin in pain field has grown rapidly during the last decades, the growth has been led primarily by observations and studies performed in the clinic
• Testing botulinum neurotoxin in pre-clinical models of pain can provide an opportunity for systematic evaluation of treatment variables and subsequent improvements in clinical study design
• Pre-clinical experiments can also help further our understanding of the mechanisms mediating therapeutic efficacy of neurotoxin in pain and in designing a range of modified neurotoxin molecules with enhanced therapeutic profiles
Mikhail Kalinichev, Executive VP Corporate Strategy, Ipsen

18.30 Co-Chairs’ Closing Remarks and Close of Day Two
**Half-Day Post-Conference Workshop A**

**Wednesday 23rd May 2018, Holiday Inn Kensington Forum, London, UK**

08.30 - 12.30

**How Should The Likely Future Pain Therapeutic Landscape Inform Current Drug Development?**

**Workshop Overview**

In response to continuing unmet need, there is a high number of novel drugs in the pain therapeutics pipeline. For those developing new drugs, it is important to consider what the future landscape is likely to look like at the time of launch and how this should inform current activities. Active participation in the workshop will be highly encouraged.

**Why should you attend?**

Delegates will be encouraged to consider how their drugs fit into a future pain therapeutics landscape and what action they should be considering now to maximise their chances of success.

**About the workshop leader**

Joanne Taylor, who has a PhD in developmental neuroscience from King’s College London, heads up Prescient’s neuroscience business. After completing a postdoctoral fellowship, she joined Eisai. Over her 18-year career there, she led global teams in the discovery of novel therapeutic strategies for neurological conditions. As Director of Strategic Research Planning, she led reviews of Eisai’s neuroscience portfolio to identify areas of major focus and investment. Since joining Prescient in 2011, Joanne has supported portfolio, clinical, regulatory and commercial strategies for a wide array of clients. She is a seasoned workshop moderator.

**Prescient Healthcare Group** is a speciality biopharmaceutical product strategy and decision support consultancy that helps our clients make better clinical and commercial decisions, resulting in improved outcomes for patients, customers and shareholders. From our offices in London, New York, San Francisco, New Delhi and Beijing, our three specialist practices provide decision support to various pharmaceutical functions (inflexionRx), develop strategies that make our clients’ assets stand out from the competition (VantageRx), and align cross-functional teams on product strategy (FusionRx).

**Agenda**

08.30 Registration and Coffee
09.00 Opening remarks and introductions
09.10 Overview of the current pain therapeutics landscape
  • Current market
  • Drugs in development
  • Regulatory challenges
  • Current value propositions
09.50 How is the pain therapeutics landscape likely to change in the next 3-5 years?
  • Novel mechanisms
  • Disruptive technologies
  • Regulatory changes
  • Future access requirements
10.30 Morning Coffee
11.00 How can drugs in development successfully differentiate in the future pain therapeutics market?
  • Critical success factors in the future market
  • Future stakeholders
  • Differentiated future value propositions
11.40 Practical steps toward future success
  • Open discussion on practical steps to plan for success in the future pain therapeutics market
12.20 Closing remarks
12.30 End of workshop

**Half-Day Post-Conference Workshop B**

**Wednesday 23rd May 2018, Holiday Inn Kensington Forum, London, UK**

13.30 - 17.30

**Clinical, Regulatory and Market Access Aspects in the Development of Medicinal Products intended for the Treatment of Pain in Europe and USA**

**Workshop Overview:**

The first section of this workshop will provide key aspects of EU and US marketing applications that have succeeded and those that have failed looking at relevant endpoints, patient populations and outcome measures.

The second part of the workshop will focus on Market Access opportunities and unmet need for new medicinal products intended for the treatment of pain in Europe and USA.

**Why should you attend?**

• This interactive workshop will introduce participants to a 360° approach to Regulatory challenges and opportunities related to the development of Pain Treatment Products

• The workshop will illustrate Clinical Development aspects aimed at the successful design and execution of clinical studies through an analysis of unmet needs, endpoints and outcomes

• You will finally be able to gather insights on current treatment practice and Market drivers for future Neuropathic, Chronic and Post-Operative Pain treatment products

**About the host:**

Simon Ruini is Managing Director of Pharma Design Limited, a boutique service provider for biotechs in achieving Marketing Authorisations in Europe and preparing adequately for Market launch. The Company provides assistance with Clinical Study design, Marketing Applications and Drug Safety services (i.e. Pharmacovigilance) during drug development and post-marketing.

**Pharma Design** is a small service provider with a network of specialised consultants assisting Pharmaceutical Companies & Biotechs in achieving Marketing Authorisations in Europe and preparing adequately for Market launch. The Company provides assistance with Clinical Study design, Marketing Applications and Drug Safety services (i.e. Pharmacovigilance) during drug development and post-marketing.

**Agenda**

13.30 Registration and Coffee
14.00 Opening remarks and introductions
14.10 Guidelines and Regulatory Aspects regarding Clinical Development of products intended for the treatment of pain
  • Comparison of guidelines and regulatory aspects in EU and USA
  • Definitions and indications
  • EMA and FDA Guidance
  • Claims and labelling
  • Limitations of established pain classifications
14.50 Clinical Study design for the development of products intended for the treatment of pain
  • Clinical endpoints
  • Choice of comparators
  • Patient Populations
  • Outcome measures
  • Unmet needs
15.30 Afternoon Tea
16.00 Recent License Approvals in EU and USA
  • Recent EMA and FDA License approvals
  • What has convinced regulators?
  • What has not convinced regulators?
16.40 Inflammatory, Chronic and Post-operative pain Treatments - Market opportunities in EU and U.S.A.
  • Patient Journeys
  • Market objectives
  • Prescribing trends in EU and USA
17.20 Closing Remarks
17.30 End of Workshop