

# Entereg<sup>®</sup> (alvimopan) Capsules

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United States Food and Drug Administration  
Gastrointestinal Drugs Advisory Committee Meeting

January 23, 2008

# Entereg<sup>®</sup> (alvimopan) Capsules

## Introduction

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**Linda Young, RPh, JD**

**Vice President of Regulatory Affairs  
Adolor Corporation**

## Proposed Indication

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- ❖ **ENTEREG<sup>®</sup> (alvimopan) is indicated to accelerate the time to upper and lower gastrointestinal recovery following partial large or small bowel resection surgery with primary anastomosis**

## Postoperative Ileus (POI)

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- ❖ A serious medical condition that affects patients and the healthcare system
- ❖ Contributes to postoperative morbidity
  - Most common cause for delayed hospital discharge following bowel resection
- ❖ No FDA-approved agent for the management of POI
  - Important unmet medical need

## Entereg<sup>®</sup> (alvimopan) Capsules

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- ❖ **Novel drug in a new class**
- ❖ **A peripherally acting mu-opioid receptor antagonist for the management of postoperative ileus after bowel resection**
- ❖ **Mitigates the adverse side effects of opioid analgesics on the GI tract without blocking their beneficial analgesic effects**

## Entereg<sup>®</sup> Development

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- ❖ Since April 2002, Adolor has worked with GlaxoSmithKline (GSK) on development of Entereg<sup>®</sup>
  - Adolor for the acute-care POI indication (in-patient setting)
  - GSK for the chronic-care OBD indication (out-patient setting)

# Entereg<sup>®</sup> Regulatory Development

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- ❖ Initial NDA 6/2004
- ❖ Three phase III studies (302, 308, 313)
  - BR and TAH
  - Variability in response for combined population
  - Consistent response in BR subgroup
- ❖ Study 001, conducted ex-US with different clinical practice

## Entereg<sup>®</sup> Regulatory Development

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- ❖ **Approvable letter July 2005**
  - **Additional study for efficacy in BR only—  
Study 314**
- ❖ **Complete response submitted May 2006**
- ❖ **Approvable letter November 2006**
  - **GSK014 final results**
  - **Risk management plan**
- ❖ **Complete response August 2007**

## Presentation Overview

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- ❖ **Clinically meaningful benefit in patients undergoing BR surgery**
  - Large robust efficacy database in BR
- ❖ **Favorable safety profile in POI**
  - Worldwide POI safety population = 2610
- ❖ **Entereg<sup>®</sup> fulfills an unmet medical need**

# Today's Agenda

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**POI, a Surgical  
Perspective**

**Anthony Senagore, MD, MS, MBA  
Spectrum Health**

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**POI Clinical  
Development and  
Efficacy**

**Lee Techner, DPM  
Adolor Corporation**

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**OBD Study GSK014  
Safety Findings**

**Eric Mortensen, MD, PhD  
GlaxoSmithKline**

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**POI Safety  
Risk Management  
Plan**

**David Jackson, MD  
Adolor Corporation**

## Consultants

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**John Alexander, MD**  
**Duke University School of Medicine**

**John Camm, MD, FRCP, FESC, FACC**  
**St. George's Hospital Medical School**

**Conor Delaney, MD, PhD, FACS**  
**University Hospitals of Cleveland**

**Charles Fuchs, MD, MPH, FACP**  
**Dana-Farber Cancer Institute**

**Gary Koch, PhD**  
**University of North Carolina**

**Kenneth W. Lyles, MD**  
**Duke University School of Medicine**