



**Entereg<sup>®</sup> (alvimopan) Preliminary  
Findings from Study 767905/014 and  
Clinical Development Program Update**

**April 9, 2007**

# Safe Harbor Statement

This oral presentation and the questions and answers that follow contain forward-looking statements, including, but not limited to, statements about:

- our ability to receive FDA approval for our NDA in POI for Entereg®
- our collaborator's plans for development of Entereg® in opioid induced bowel dysfunction
- anticipated dates of clinical trial initiation, completion, and announcement of trial results by us and our collaborators
- anticipated dates for regulatory submissions by us and our collaborators and regulatory actions
- anticipated results of clinical trials
- anticipated efforts of our collaborators
- our plans for manufacturing and supply for our products
- our research efforts
- anticipated operating losses and capital expenditures
- estimates of the market opportunity and the commercialization plans for our product candidates
- our ability to acquire or in-license products and product candidates.

These statements are subject to risks and uncertainties, known and unknown, which could cause actual results and developments to differ materially from those expressed or implied in such statements. Such known risks and uncertainties relate to, among other factors: the risk that the OBD development program remains on hold indefinitely; the risk that Adolor may not receive regulatory approval of Entereg® (alvimopan) for POI, OBD, or any other indication; the risk that Adolor may not be able to adequately address the deficiencies in the November 2006 FDA approvable letter; the risk that a risk management plan could materially adversely affect the commercial prospects for Entereg, if regulatory approval is achieved; the risk that Adolor may not obtain FDA approval for Entereg in POI, whether due to Adolor's inability to provide additional data satisfactory to the FDA to obtain approval for the NDA, the adequacy of the safety and efficacy data from all of the Entereg studies, changing regulatory requirements, the risk that the FDA may not agree with Adolor's and GSK's analyses of the Entereg studies (including Study 014) and may evaluate the results of these studies by different methods or conclude that the results from the studies, whether or not statistically significant, do not support safety, efficacy, a favorable risk/benefit profile, or there were human errors in the conduct of the studies, or otherwise; adverse safety findings in any Entereg studies; the risk that regulatory approvals for the use of Entereg in OBD are not achieved; the risk that filing targets for regulatory submissions or user fee goal dates are not met; the risk that the results of other clinical trials of Adolor's drug product candidates, including Entereg, are not positive; the risk of product liability claims; reliance on third party manufacturers; the costs, delays and uncertainties inherent in scientific research, drug development, clinical trials and the regulatory approval process; Adolor's history of operating losses since inception and its need for additional funds to operate its business; Adolor's reliance on its collaborators, including GSK, in connection with the development and commercialization of Entereg; market acceptance of Adolor's products, if regulatory approval is achieved; competition; and securities litigation.

Further information about these and other relevant risks and uncertainties may be found in Adolor's Reports on Form 8-K, 10-Q and 10-K filed with the U.S. Securities and Exchange Commission. Adolor urges you to carefully review and consider the disclosures found in its filings which are available in the SEC EDGAR database at <http://www.sec.gov> and from Adolor at <http://www.adolor.com>. Given the uncertainties affecting pharmaceutical companies in the development stage, you are cautioned not to place undue reliance on any such forward-looking statements, any of which may turn out to be wrong due to inaccurate assumptions, unknown risks, uncertainties or other factors. Adolor undertakes no obligation to (and expressly disclaims any such obligation to) publicly update or revise the statements made herein or the risk factors that may relate thereto whether as a result of new information, future events, or otherwise.

# Study 014

## Primary Objective:

To compare alvimopan with placebo for long-term safety and tolerability in patients taking opioids for chronic non cancer pain with opioid induced bowel dysfunction

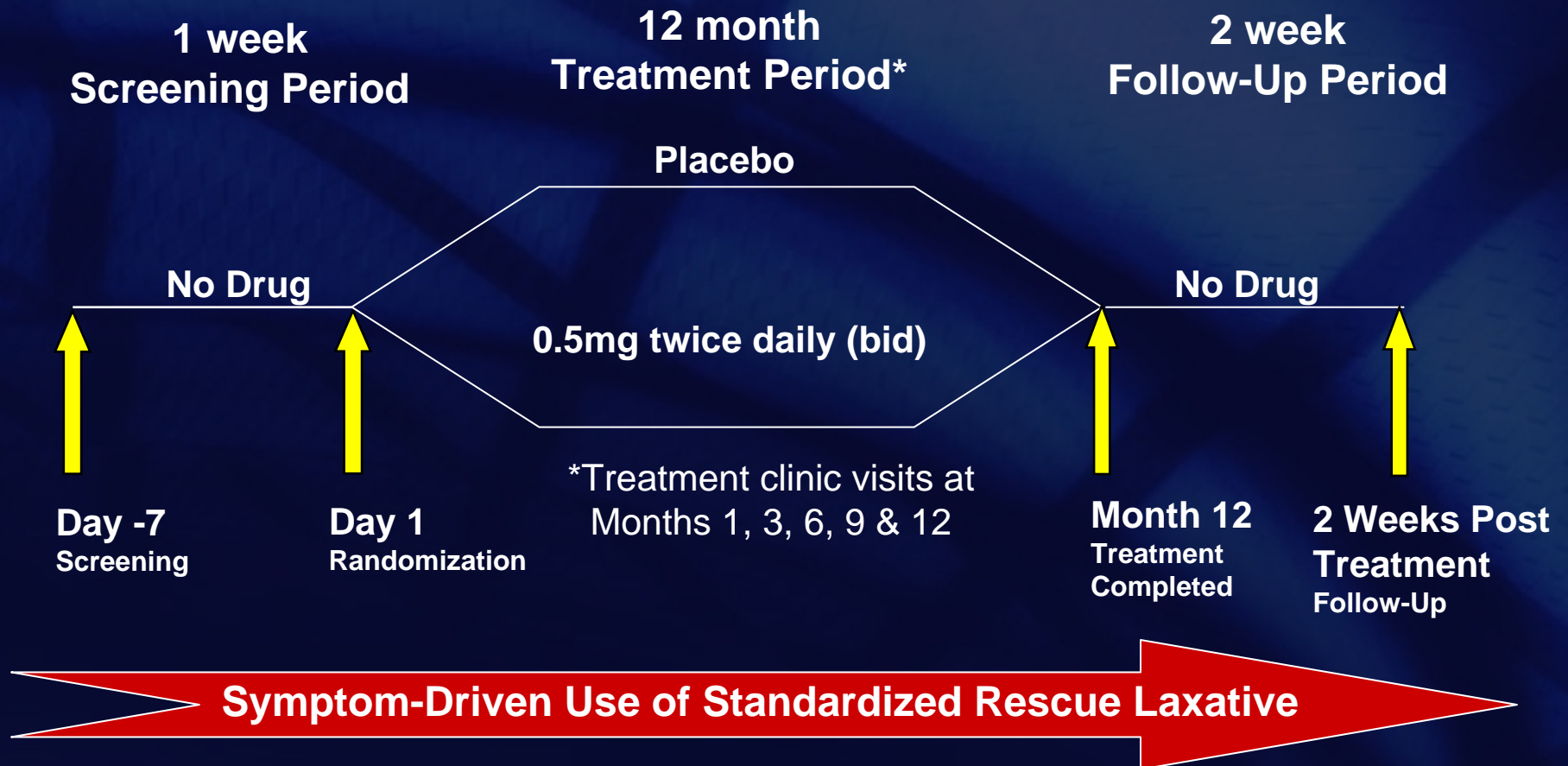
## Secondary Objectives:

To compare alvimopan with placebo for constipation related quality of life assessments

Additional safety assessments

# Study 014 Design

Randomized (2:1), double-blind, placebo-controlled, multi-country, Phase 3



# Study 014 Demographics

<b>Demographics</b>	<b>Placebo (N=267)</b>	<b>Alvimopan 0.5mg BID (N=538)</b>
Mean Age (yrs)	51.9	53.8
Caucasian (%)	87	91
Female (%) / Male (%)	37/63	35/65
BMI (kg/m <sup>2</sup> )	29.5	29.9

## Other Characteristics

Overweight / Obese (%)	67	71
Tobacco Use (%)	40	39

# Study 014 Population

## General Observations:

- Primary pain conditions
  - Back Pain, Arthritis, Fibromyalgia
- High prevalence at baseline medical conditions
  - Musculoskeletal, Cardiac, Psychiatric, Gastrointestinal
- High prevalence of CV and cancer risk factors
  - Smoking
  - Obesity
  - Hypertension
  - Hyperlipidemia
- Prevalent use of concomitant medications
  - Cardiac
  - Lipid lowering
  - Antidepressants
  - Thyroid
  - Proton pump inhibitors

# Study 014 – Most Frequent Adverse Events

	<b>Placebo</b> (N = 267)	<b>Alvimopan</b> (N = 538)
Abdominal Pain	13%	16%
Diarrhea	12%	14%
Headache	11%	10%
Nausea	11%	9%
Vomiting	6%	7%



# Cardiovascular Serious Adverse Events – OBD Studies

	<i>Study 014</i>		<i>Non-Cancer OBD Studies* (w/o Study 014)</i>		<i>Non-Cancer OBD Studies* (w/Study 014)</i>	
	Placebo (N=267)	Alvimopan (N=538)	Placebo (N=523)	Alvimopan (N=1190)	Placebo (N=790)	Alvimopan (N=1728)
Myocardial Infarction	- (0)	7 (1.30%)	2 (0.38%)	1 (0.08%)	2 (0.25%)	8 (0.46%)
All Cardiovascular SAEs	3 (1.12%)	14 (2.60%)	5 (0.96%)	14 (1.18%)	8 (1.01%)	28 (1.62%)

*\*Includes Studies 011, 012, 013, 217, and 304*

# Cardiovascular Serious Adverse Events

## Study 014 Observations

- Final results from Study 014 appear to show no additional serious cardiovascular adverse events following the interim analysis
- Cardiovascular adverse events reported in Study 014 were in patients with established or at high risk for cardiovascular disease. Risk factors included diabetes, vascular and ischemic heart disease, obesity, smoking, hypertension and preexisting cardiovascular disease
- The incidence of cardiovascular adverse events in Study 014 appears consistent with epidemiological expectations for the subject population
- The timing of events does not appear to be linked to duration of dosing. While Study 014 (12-month study) was the first evaluation of alvimopan treatment beyond twelve weeks, the majority of reported CV SAEs occurred in subjects on alvimopan treatment ranging from 30 days to 112 days
- 5 of 7 MIs occurred at 2 investigational study sites

# Cardiovascular Serious Adverse Events - POI Studies

## POI Studies\*

Event	Placebo (N=1365)	Alvimopan All Doses (N=2610)
Myocardial Infarction	0.51%	0.50%
Other CV Adverse Events of interest	3.37%	2.45%

*\*Includes Studies 206, 213, 214, 302, 306, 308, 313, 314 and 001*

# Cardiovascular Serious Adverse Events

*Does alvimopan, a mu opioid receptor antagonist, unmask cardioprotective effects of opioids?*

- Cardioprotective effects of opioids have been hypothesized to be mediated by delta receptors (preclinical models)
- Alvimopan and its metabolite bind with higher selectivity to the mu receptor over delta and kappa (selectivity >20-100 fold)
- Binding data, together with PK data, do not support mechanism – based antagonism that would reverse cardioprotective effects

# Neoplasm Serious Adverse Events

## Malignant Neoplasm

Non-Cancer OBD Studies	Placebo	Alvimopan All Doses
Study 014	1/267 (0.4%)	4/538 (0.7%)
Studies 011, 012, 013	0/465	1/1060 (0.09%)

### Study 014 - All Neoplasms\*:

Placebo	2	(0.7%)
Alvimopan	15	(2.8%)

*\*benign, malignant, skin cancers and unspecified, including polyps*

# Neoplasm Events

*Do opioid ligands inhibit the induction or proliferation of cancer?*

- No clinically relevant findings with alvimopan in rodent carcinogenicity studies
- Literature Review
  - Opioid growth factor (OGF): An endogenous opioid peptide believed to mediate inhibition of cell proliferation and differentiation
  - Small molecule opioid receptor agonists (e.g., morphine) do not interact with OGF receptor to inhibit cell proliferation
  - Mu and delta receptors do not resemble OGF receptors at either molecular or protein level, nor do mu, delta or kappa agonists appear to compete with this receptor
  - Mu opioid receptor antagonists have been shown to inhibit angiogenesis suggesting possible positive impact on cancer treatment

# Quality of Life Assessment

- PAC-QOL demonstrated a positive benefit of alvimopan compared to placebo
- Each subcategory of assessment also showed a positive difference compared to placebo
  - Physical discomfort
  - Psychosocial discomfort
  - Worries and concerns
  - Dissatisfaction

# Alvimopan Development

## GSK

- Study 015 Protocol withdrawn
- Study 684 (Extension of Study 008) stopped

## Adolor

- Study 228 (Combination Program) enrollment suspended
- POI Complete Response targeted 2Q 2007





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