

# Tapentadol IR Phase 3 Clinical Trial Overview

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Web Cast  
Friday, May 9, 2008

# Web Cast Agenda

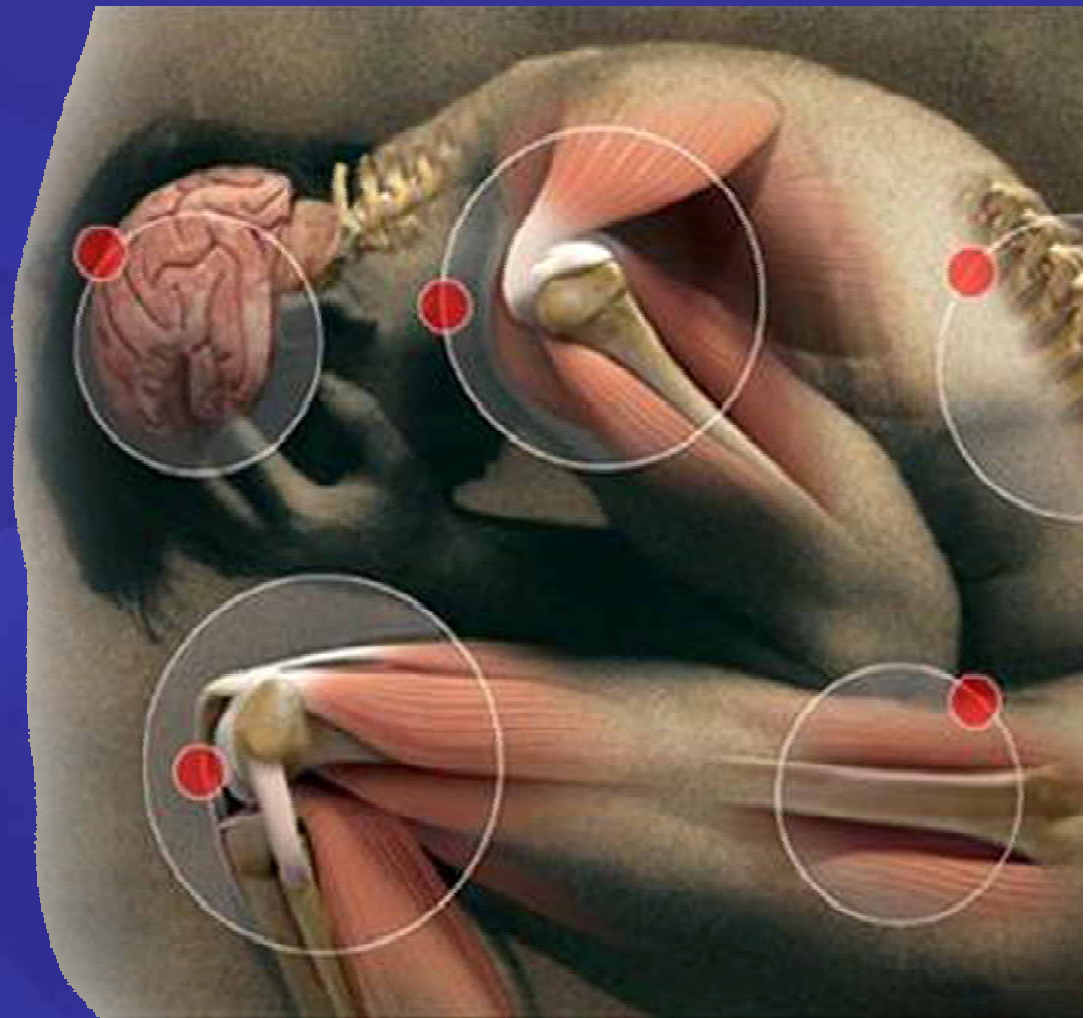
- Overview of Pain Management, overview of tapentadol
  - Christine Rauschkolb, M.D., Ph.D., Senior Director, Team Leader for Compound Development, Johnson & Johnson Pharmaceutical Research and Development, L.L.C. (J&JPRD)
- Overview of Phase 2 data
  - David Upmalis, M.D., Senior Director, CNS/Pain, J&JPRD
- Clinical Phase 3 study data details
  - Charles Oh, M.D., Director, J&JPRD
  - David Upmalis, M.D., Senior Director, CNS/Pain, J&JPRD
- Conclusion

# Note on Forward Looking Statements

- [This Web cast contains "forward-looking statements" as defined in the Private Securities Litigation Reform Act of 1995. These statements are based on current expectations of future events. If underlying assumptions prove inaccurate or unknown risks or uncertainties materialize, actual results could vary materially from Johnson & Johnson's expectations and projections. Risks and uncertainties include general industry conditions and competition; economic conditions, such as interest rate and currency exchange rate fluctuations; technological advances and patents attained by competitors; challenges inherent in new product development, including obtaining regulatory approvals; domestic and foreign health care reforms and governmental laws and regulations; and trends toward health care cost containment. A further list and description of these risks, uncertainties and other factors can be found in Exhibit 99 of the Company's Annual Report on Form 10-K for the fiscal year ended December 30, 2007. Copies of this Form 10-K, as well as subsequent filings, are available online at [www.sec.gov](http://www.sec.gov) <<http://www.sec.gov>>, [www.jnj.com](http://www.jnj.com) or on request from Johnson & Johnson. Johnson & Johnson does not undertake to update any forward-looking statements as a result of new information or future events or developments.]

# Key Trends in Pain Management

- Pain management today is suboptimal
- Variable efficacy from patient to patient
- Side effects may result in under-treatment
- Need better treatments
  - Improved side effect profile
  - Longer duration of action



# Pathways of Pain

Multimodal treatments that address more than one pathway may provide more comprehensive pain relief<sup>1-3</sup>

Just as pain travels along multiple pathways, so should pain relief

An agent that inhibits ascending pathways<sup>3,4</sup>

- Opioid
- Local anesthetic
- Antiepileptic
- NSAID/acetaminophen
- $\alpha_2\delta$  ligand
- NMDA antagonist



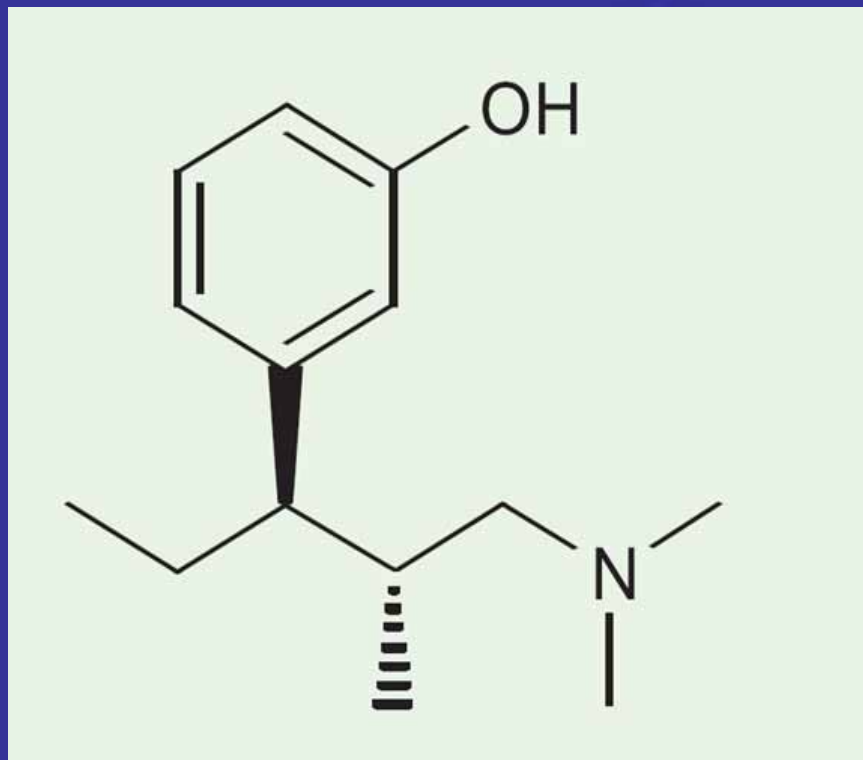
An agent that enhances descending pathways<sup>4,5</sup>

- Norepinephrine reuptake inhibitor
- Serotonin reuptake inhibitor
- Tricyclic antidepressant
- Opioid

For more information on this and other topics in pain management, visit: [www.medscape.com/infosite/paininstitute](http://www.medscape.com/infosite/paininstitute)

- Ascending pathways transmit pain signals from the periphery of the body
- Complimented by descending pain inhibiting pathways

# Tapentadol: Novel Centrally Acting Oral Analgesic



- Unique profile with two mechanisms of action in one molecule:
  - Mu-opioid receptor agonist + NE reuptake inhibitor
- Phase 3
  - Acute and chronic moderate-to-severe pain
  - Acute pain IR formulation
  - Chronic pain ER formulation
  - Acute pain IR NDA submitted to FDA, January 23, 2008
- Favorable GI profile
- Tamper-resistant formulation (ER) is in development
- Expected to be Scheduled
- Joins a long-standing pain franchise

*Co-development with Grünenthal*

# Acute Pain Phase 2 Studies Overview

- Phase 2 trials were positive
  - Dental pain (2 studies, acute, IR formulation)
  - Bunionectomy (3 studies, acute, IR formulation)
- Key takeaways of Phase 2 data:
  - The results of these studies demonstrated that tapentadol IR is effective for the relief of moderate to severe pain
  - The data also suggested that tapentadol has an improved gastrointestinal profile
- Results warranted further investigation

# Phase 3 Clinical Studies

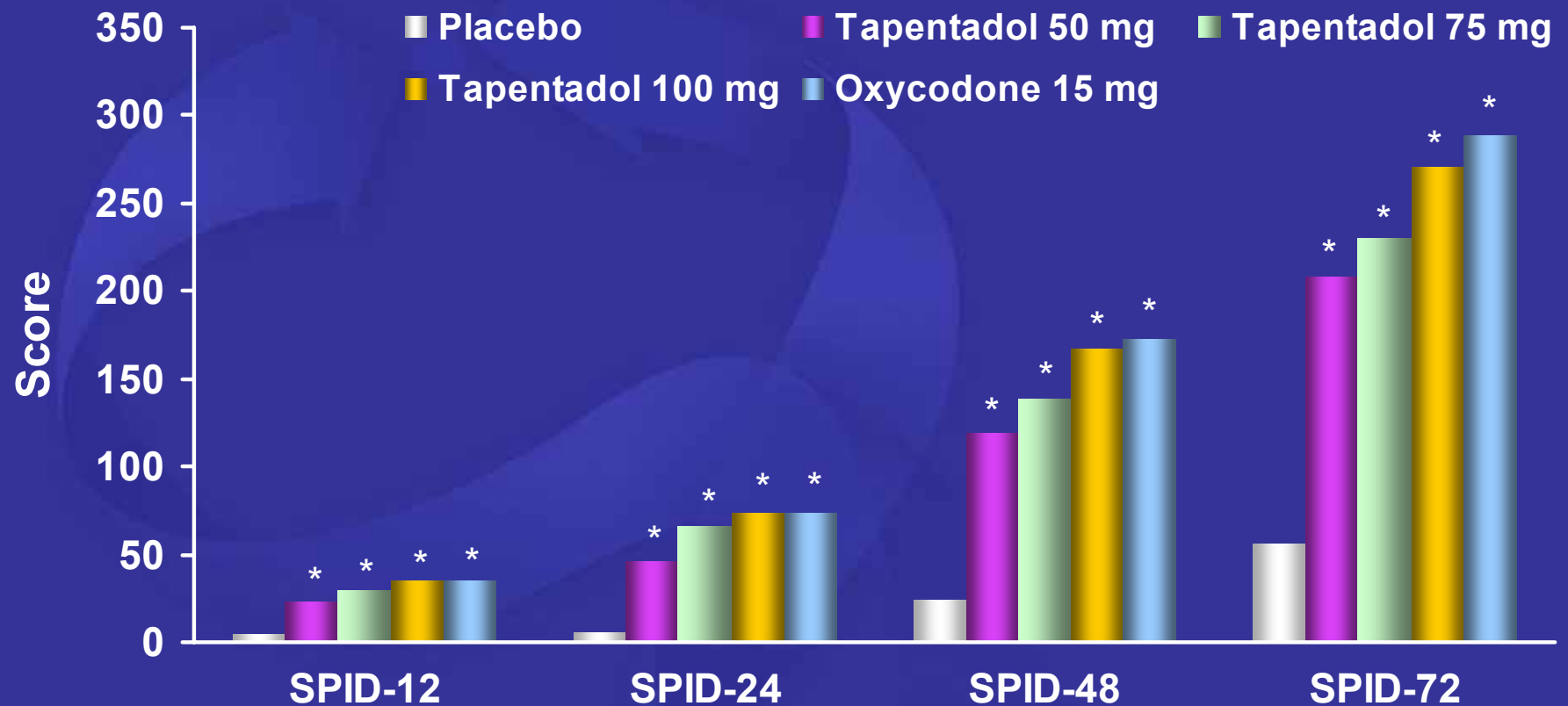
# Phase 3 Overview

<b>Study</b>	<b>Tapentadol Doses (mg)</b>	<b>Oxycodone Doses (mg)</b>	<b>Duration</b>	<b>F/M(%)</b>	<b>Mean Age (y)</b>	<b>Median Pain Score at Entry</b>
<b>Bunionectomy (N=602)</b>	<b>50, 75, 100</b>	<b>15</b>	<b>3 days</b>	<b>87/13</b>	<b>44.3</b>	<b>7.0</b>
<b>End-Stage Joint Disease (N=659)</b>	<b>50, 75</b>	<b>10</b>	<b>10 days</b>	<b>49/51</b>	<b>61</b>	<b>7.1</b>
<b>Safety (N=849)</b>	<b>50-100</b>	<b>10-15</b>	<b>Up to 90 days</b>	<b>55/45</b>	<b>56</b>	<b>6.7</b>



# PAI-3003 Bunioneectomy Study

# Primary (**SPID-48**) and Secondary (SPID-12, 24 and 72) Endpoints

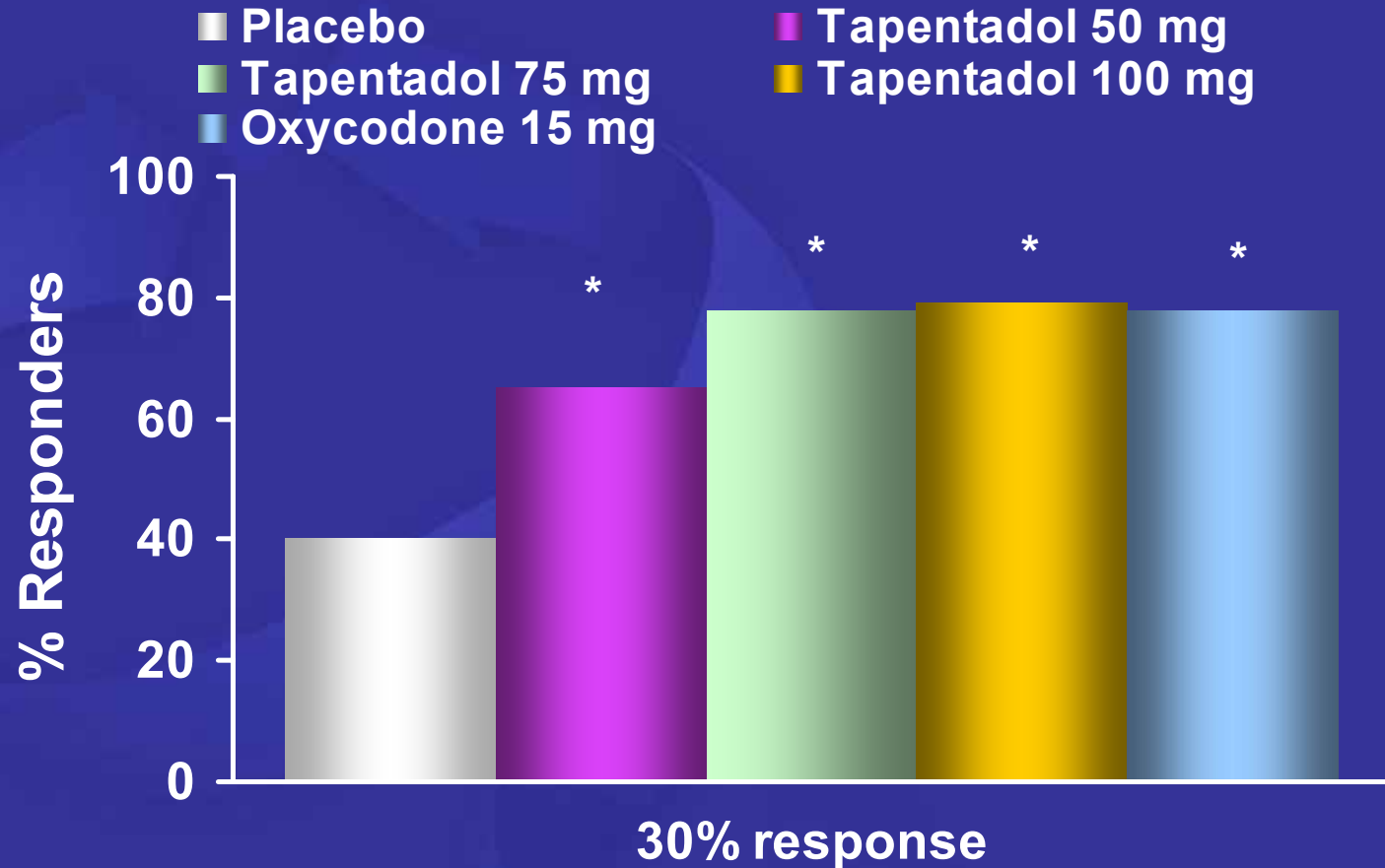


SPID = sum of pain intensity differences

\* $P < 0.001$  vs placebo

PAI-3003

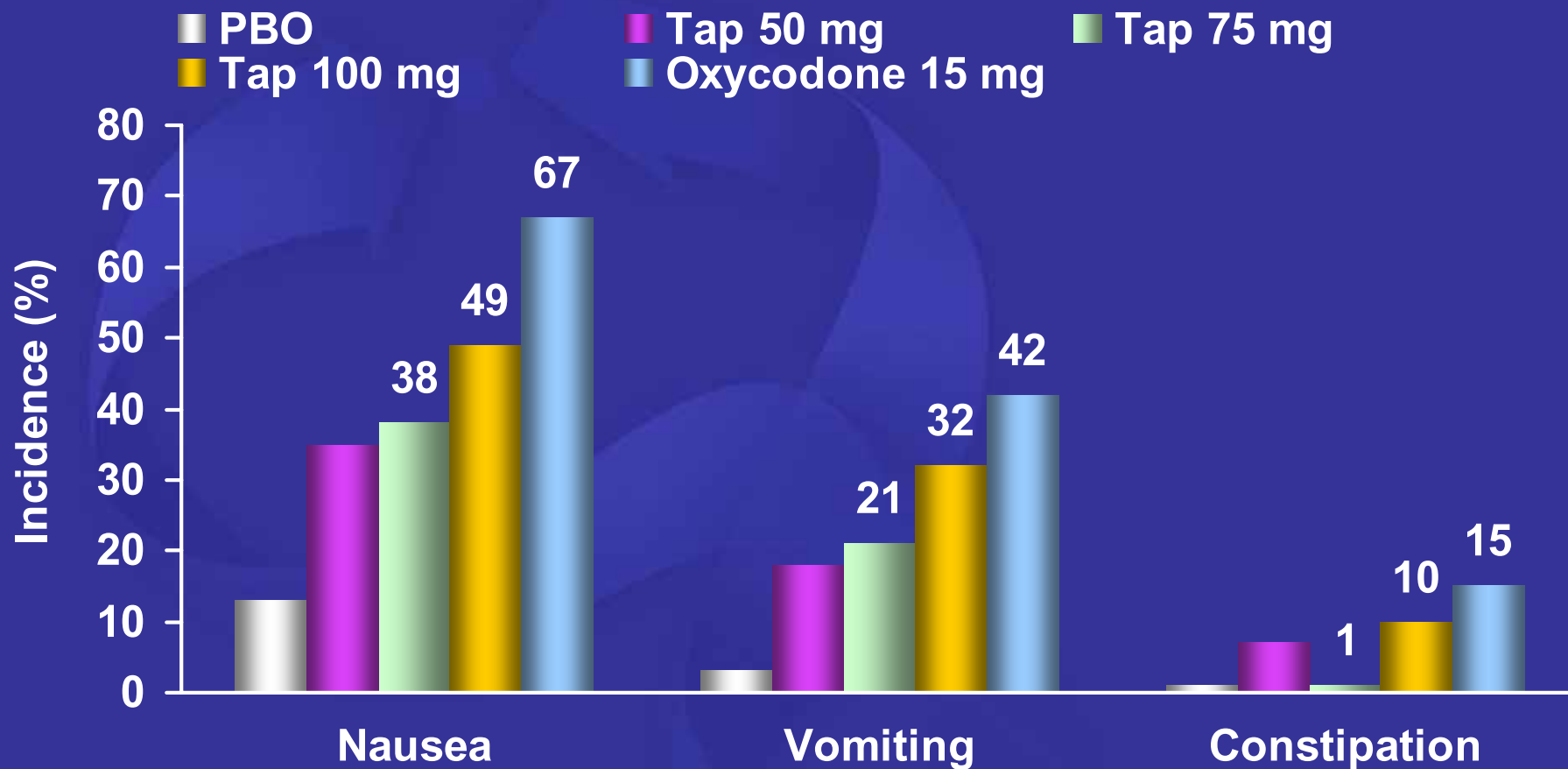
# Responder Rates Using Pain Intensity at 48 Hours



\* $P < 0.001$  vs placebo.

PAI-3003

# Incidence of GI AEs



# Incidence of CNS AEs



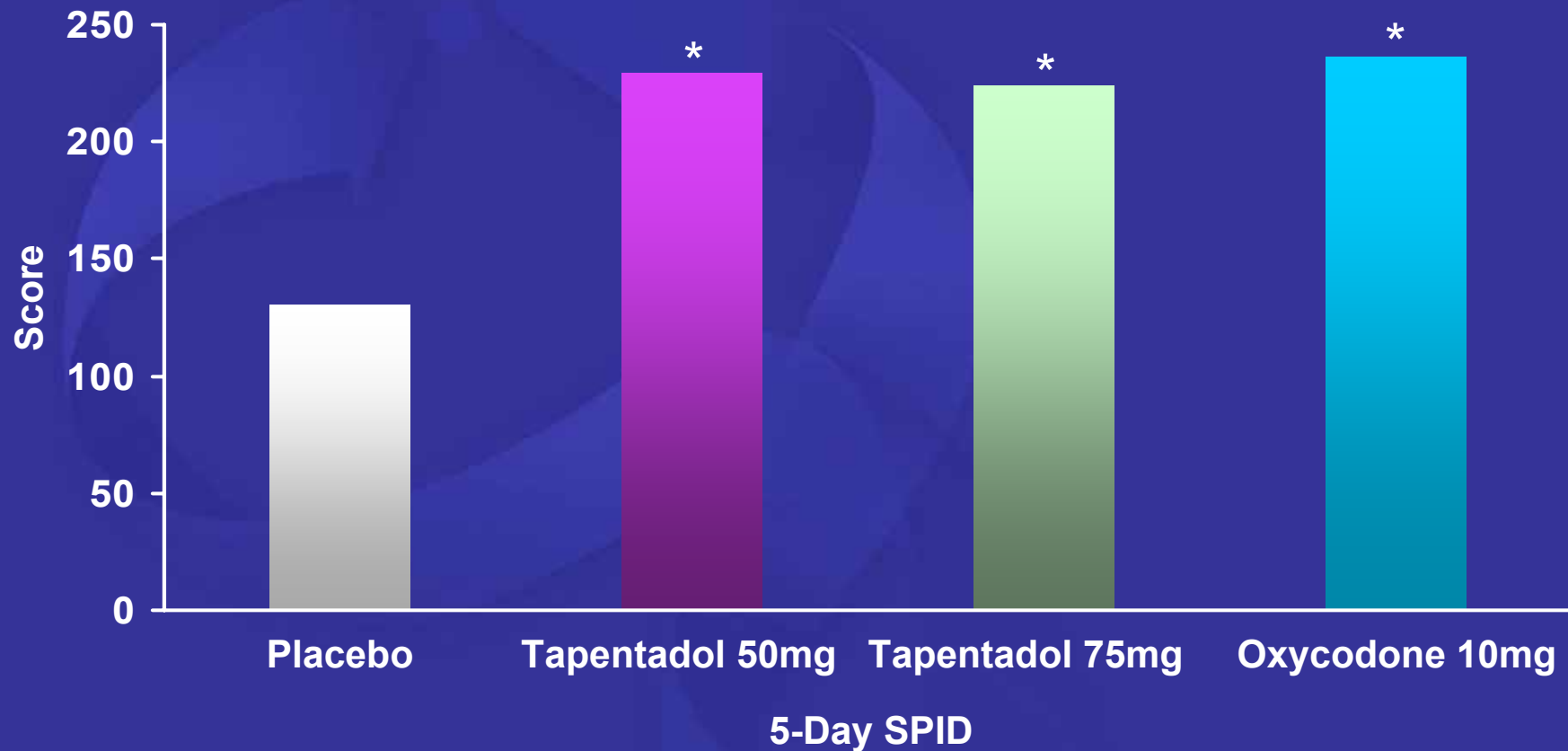
*The higher incidence of somnolence with the tapentadol IR 100 mg dose has not been observed outside the postoperative setting, and warrants further evaluation.*

PAI-3003



# **PAI-3002: End-Stage OA Hip and Knee**

# Primary Efficacy – 5-Day SPID

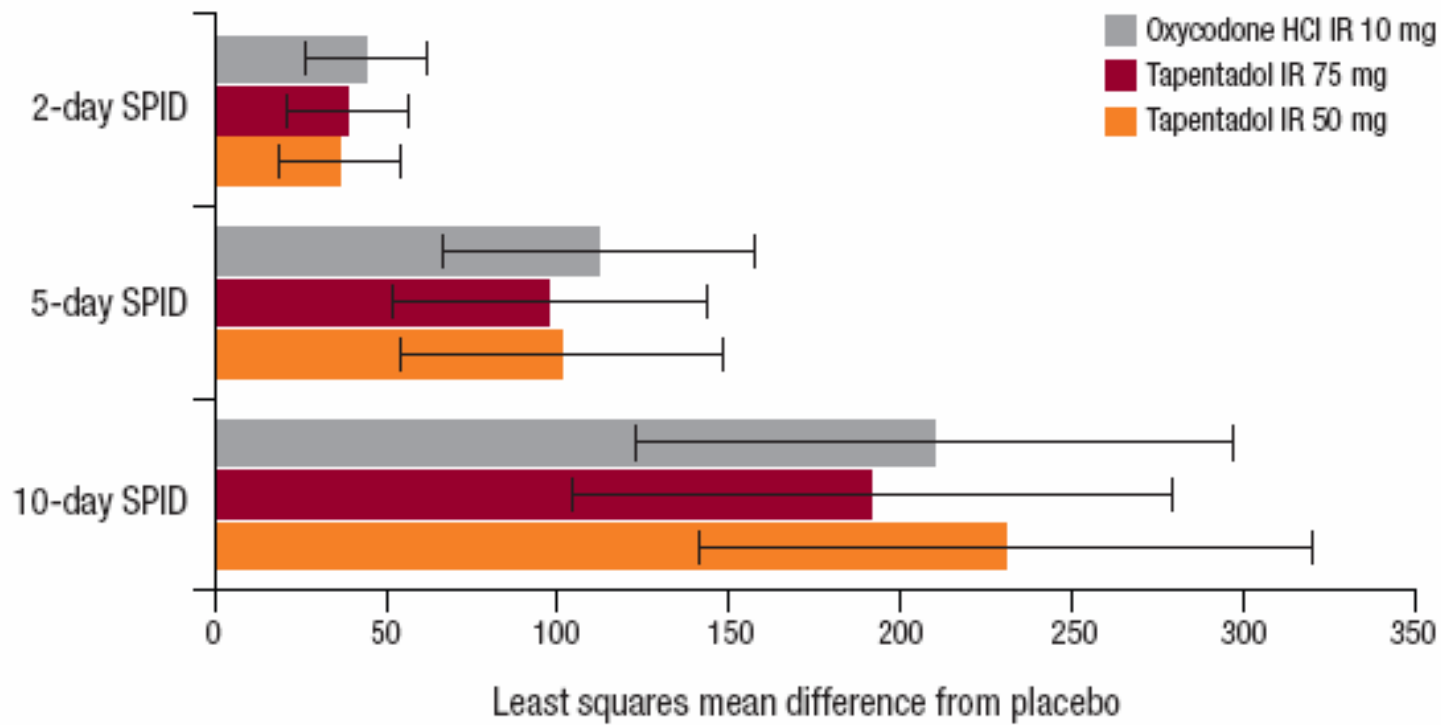


SPID = sum of pain intensity differences  
\* $P < 0.001$  vs placebo

PAI-3002

16

# Least Squares Mean Difference from Placebo for 2-day, 5-day and 10-day SPID



SPID, sum of pain intensity difference; IR, immediate release.

# Treatment Emergent AEs >5%

	<b>Placebo (n=169)</b>	<b>Tapentadol 50 mg (n=153)</b>	<b>Tapentadol 75 mg (n=166)</b>	<b>Oxycodone 10 mg (n=171)</b>
	<b>n (%)</b>	<b>n (%)</b>	<b>n (%)</b>	<b>n (%)</b>
<b>Total subj. /AEs</b>	54 (32)	81 (52)	120 (71)	144 (84)
<b>Nerv. Sys. Dis.</b>	<b>18 (11)</b>	<b>46 (29)</b>	<b>69 (41)</b>	<b>64 (37)</b>
Dizziness	8 (5)	29 (18)	44 (26)	40 (23)
Somnolence	2 (1)	10 (6)	17 (10)	21 (12)
Headache	10 (6)	10 (6)	14 (8)	5 (3)
<b>GI Disorders</b>	<b>28 (17)</b>	<b>46 (29)</b>	<b>68 (40)</b>	<b>119 (69)</b>
Nausea	9 (5)	29 (18)	35 (21)	70 (41)
Vomiting	7 (4)	11 (7)	23 (14)	59 (34)
Constipation	4 (2)	7 (4)	11 (7)	45 (26)
Diarrhea	5 (3)	5 (3)	5 (3)	5 (3)
<b>Pruritus</b>	<b>1 (1)</b>	<b>3 (2)</b>	<b>8 (5)</b>	<b>26 (15)</b>

# PAI-3004 90-Day Safety Study

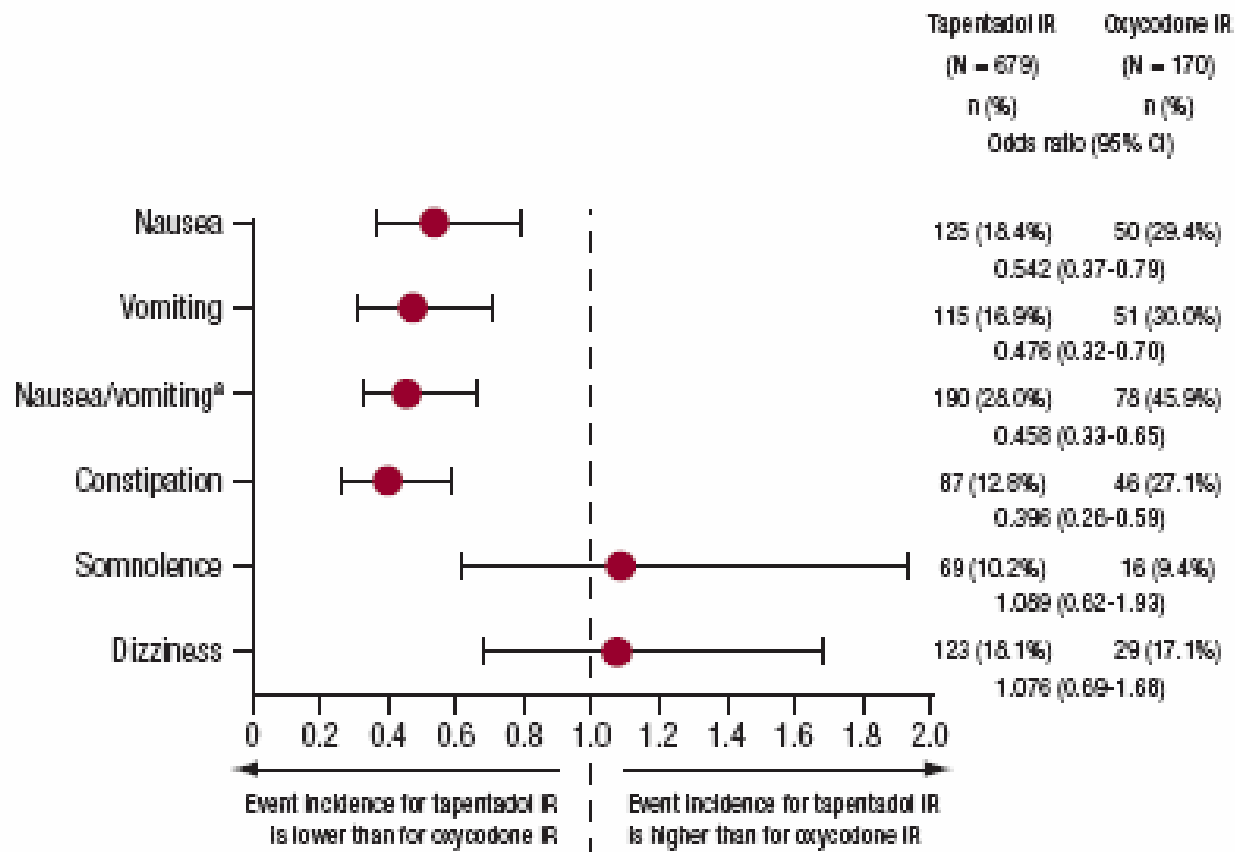
# Study Design

- Investigated the tolerability of long-term exposure, 90-days, to tapentadol IR in 878 patients with low back pain from osteoarthritis of the knee and hip
- Patients treated with a flexible dose of 50MG or 100MG of tapentadol IR every 4-6 hours, as needed, up to a maximum of 600 MG/day
- Alternatively, flexible dose of 10MG or 15MG of oxycodone IR every 4-6 hours, as needed

# Adverse Events in $\geq 5\%$ of Patients

	Tapentadol IR (50 mg – 100 mg)	Oxycodone IR (10 mg – 15 mg)
	n=679 (%)	n=170 (%)
<b>Nausea</b>	<b>18.4</b>	<b>29.4</b>
<b>Vomiting</b>	<b>16.9</b>	<b>30.0</b>
<b>Constipation</b>	<b>12.8</b>	<b>27.1</b>
Diarrhea	6.6	5.9
Dry Mouth	5.3	2.9
Dizziness	18.1	17.1
Headache	11.5	10.0
Somnolence	10.2	9.4
Fatigue	5.6	2.4
Pruritus	4.3	11.8

# Odds Ratio and 95% Confidence Intervals for Adverse Events



IR, immediate release; CI, confidence interval.

\*Composite of nausea/vomiting means an event of nausea or vomiting.

# Conclusion

## Tapentadol: Distinct Clinical Advantages

Desired Characteristics of Pain Medications	Traditional Opioids	Tapentadol
High Potency in Reducing Pain	✓	✓
Novel Mechanism of Action		✓
Minimal Drug Interaction		✓
Improved GI Tolerability		✓

# Questions

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**Thank You!**