



**Analyst & Investor Briefing**  
*American College of Rheumatology*

*October 28, 2008*

# Forward-Looking Statements and Non-GAAP Financial Information

- Discussions at this meeting will include forward-looking statements. Actual results could differ materially from those projected in the forward-looking statements. The factors that could cause actual results to differ are discussed in Pfizer's 2007 Annual Report on Form 10-K and in our reports on Form 10-Q and Form 8-K
- Also, discussions during this meeting may include certain financial measures that were not prepared in accordance with generally accepted accounting principles. Reconciliations of those non-GAAP financial measures to the most directly comparable GAAP financial measures can be found in Pfizer's Current Report on Form 8-K dated October 21, 2008
- These reports are available on our website at [www.pfizer.com](http://www.pfizer.com) in the "Investors—SEC Filings" section





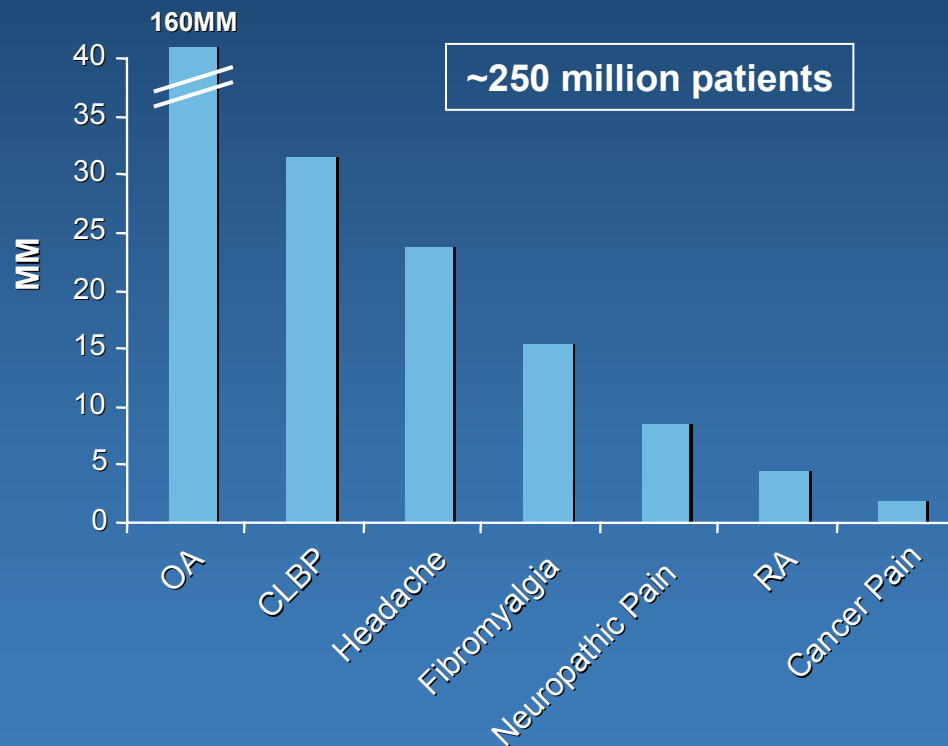
**Ken Verburg, Ph.D.**

***Development Head for Pain Therapeutics***

*October 28, 2008*

# Chronic Pain Population Continues to Expand While Unmet Needs Continue to Increase

Prevalence of Chronic Pain  
Major Global Markets (2011)



## Decision Resources

Stewart et al., Lost Productive Time and Costs Due to Common Pain Conditions in the US Workforce. *JAMA* 2003;290:2443-2454

- Steady growth in patients in chronic pain reflects aging population
- Physicians express displeasure with the current therapies
  - *“Currently medications have very low efficacy – only 1/5 patients are treated successfully – if you had this type of efficacy in another field of medicine, it would NOT be accepted. We accept it because we have nothing better.”*
- Onset of chronic pain can be life-altering and long lasting
  - Arthritis and back pain are the leading causes of disability



# Few Existing Therapeutic Classes

>50% of Patients Report These Therapies to Be Suboptimal in Relieving Their Pain\*

- **Acute Pain/  
Musculoskeletal Pain**

- Acetaminophen
- NSAIDs
- Opiates
- Local anesthetics
- Muscle relaxants

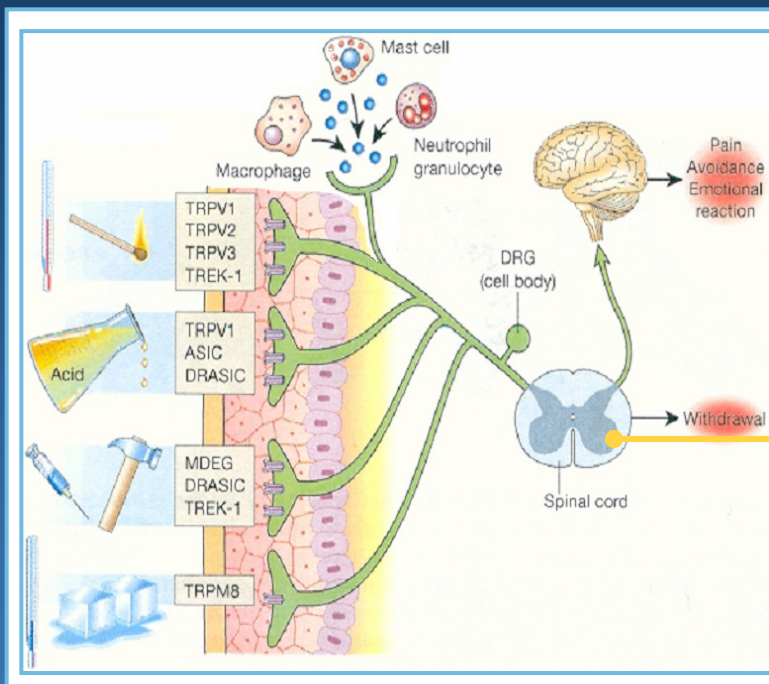
- **Neuropathic Pain**

- Anti-depressants
- Anti-epileptics
- Topical capsaicin
- Local anesthetics

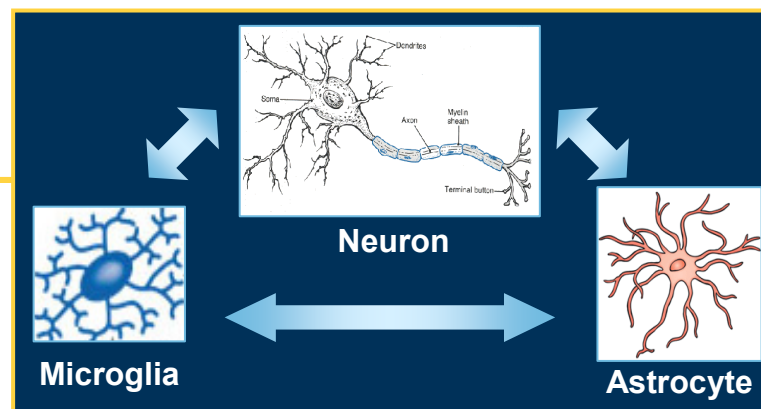


\* Mantyselka et al., *JAMA* 2003;290:2435-2442  
Stewart et al., *JAMA* 2003;290:2443-2454  
Decision Resources Report, Chronic Pain – Key Populations,  
Market Size and the Driving Force for Drug Reformulations. Oct, 2005

# Going Beyond Traditional Analgesic Drugs

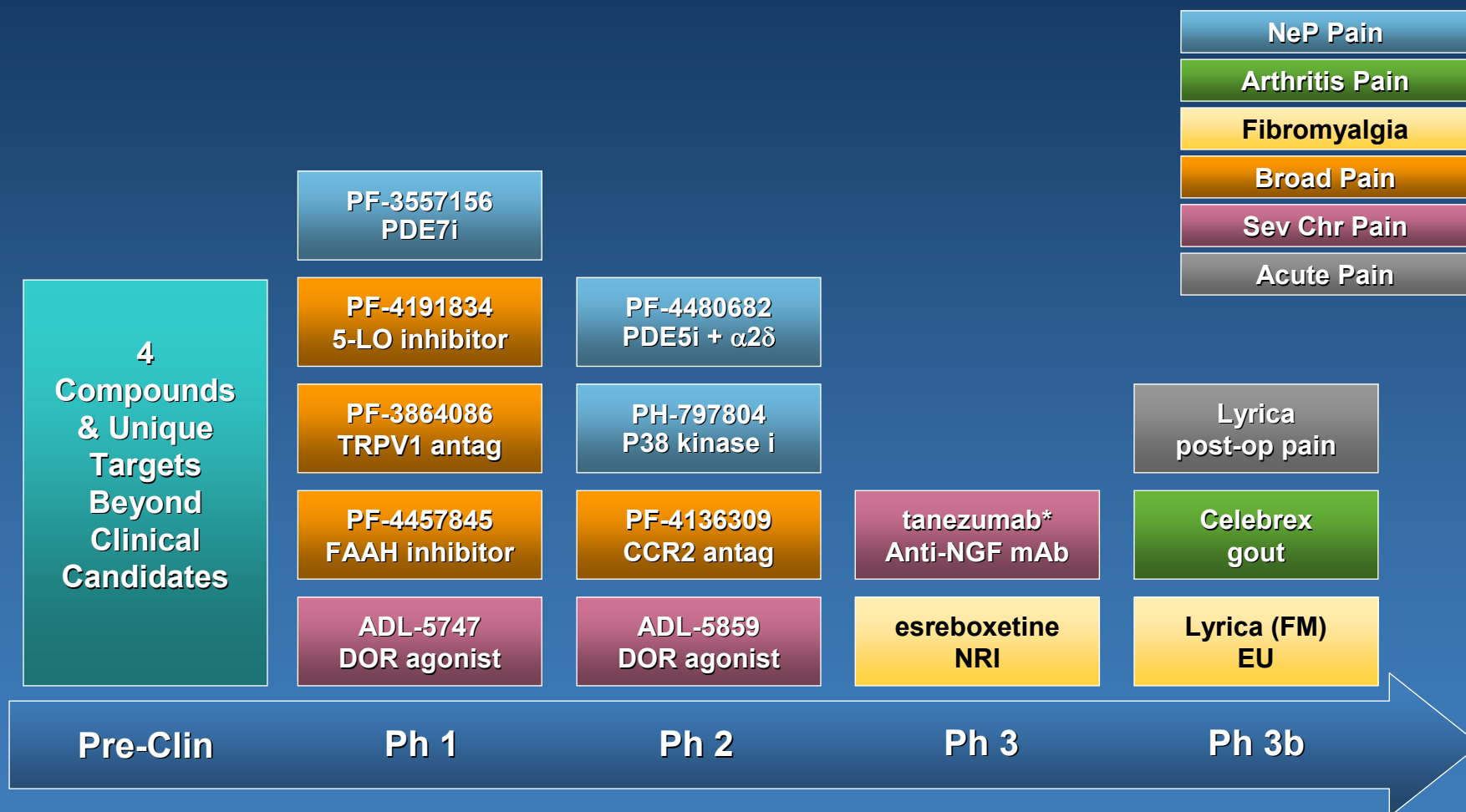


- Transduction
- Conduction
- Transmission
- Processing/perception
- Modulation
- Sensitization



# Pain Portfolio: Oct '08

## Progress to Innovative Medicines

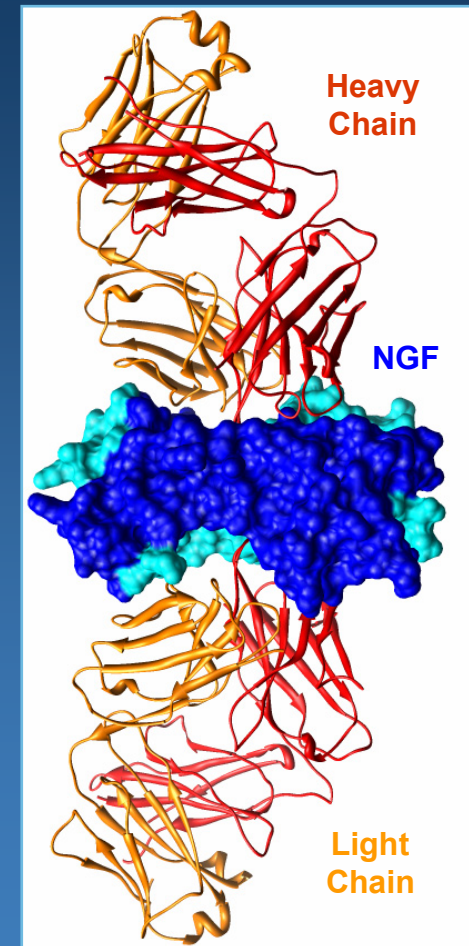


\*Projected start 4Q; OA



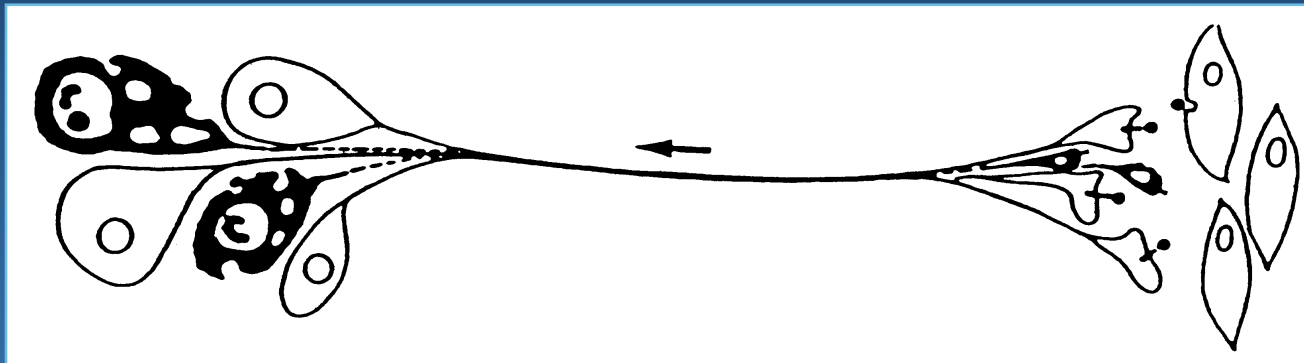
# Tanezumab: Overview

- Nerve growth factor (NGF)
  - Key pain mediator in pain
- Humanized, IgG2 monoclonal antibody
  - High specificity and affinity for NGF
  - Fc mutation limits Ab-dependent cell mediated toxicity & complement activation
- Efficacy in multiple preclinical models of pain
- Clinical efficacy demonstrated in OA
  - 5 min IV administration – (slow IV push)
  - Low projected dose  $\leq 10$  mg q 8 wks
  - Phase 3 (IV) Program: on plan to start 2008
- Program Objectives
  - Initial path to approval with OA (IV)
    - Projected BLA submission; 2011/12
  - Followed by OA (SC) & Chronic Pain (SC)



# Neurotrophic Factors (Neurotrophins)

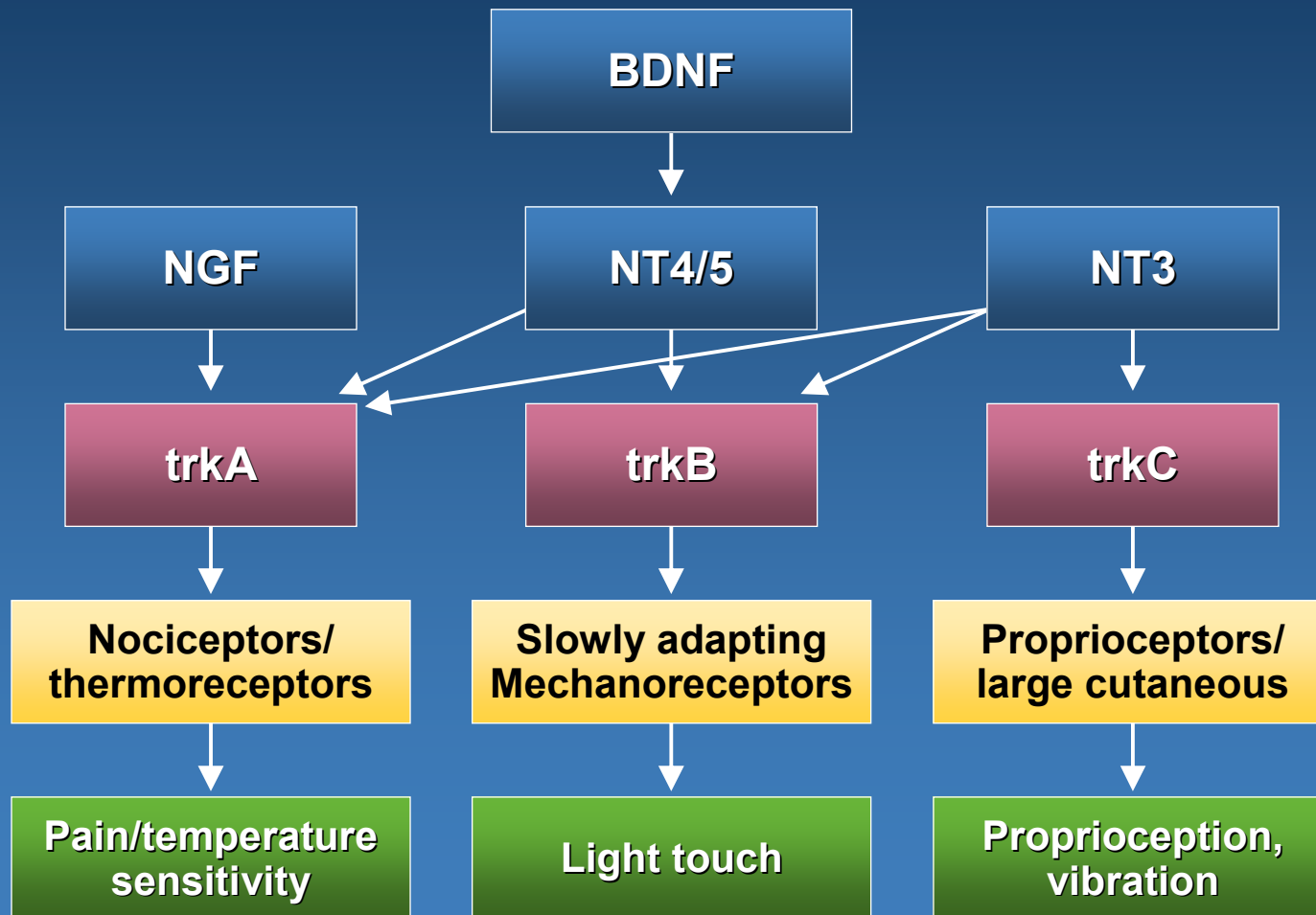
- A substance that controls neuronal maturation & survival during development of functional contacts (neuronal circuits)



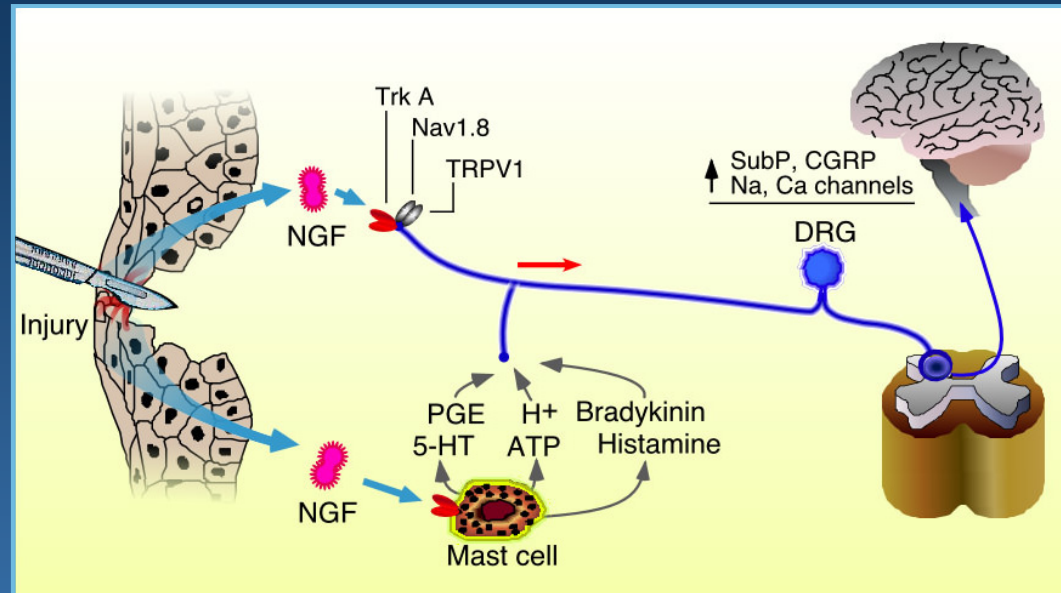
*But practically,*

- Neurotrophic factors have effects on adult neurons
  - Upregulate sensitivity, transmitter synthesis/release
  - Protect from metabolic, chemical, viral or physical insult
  - Induce/increase sprouting/regeneration

# Neurotrophins and Their Receptors on Sensory Neurons

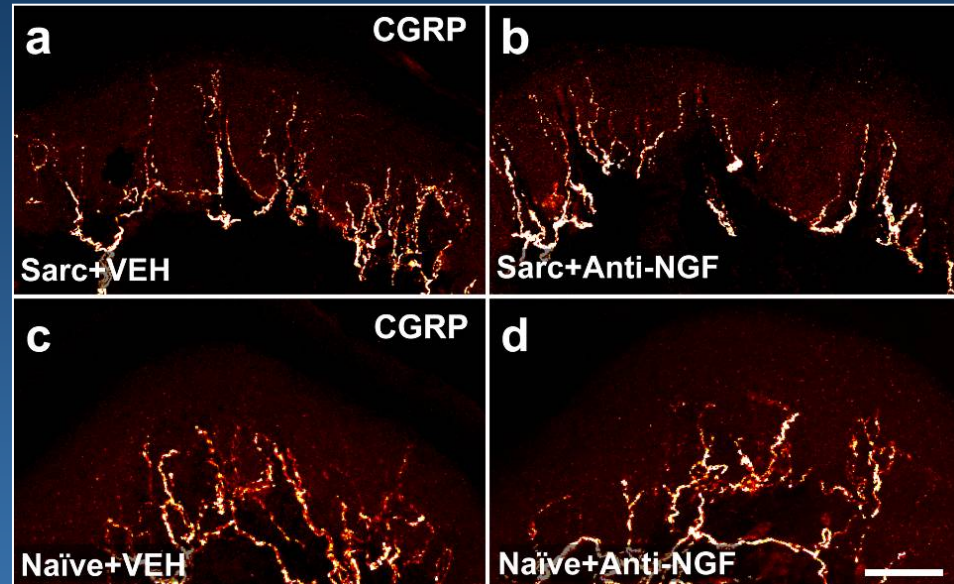
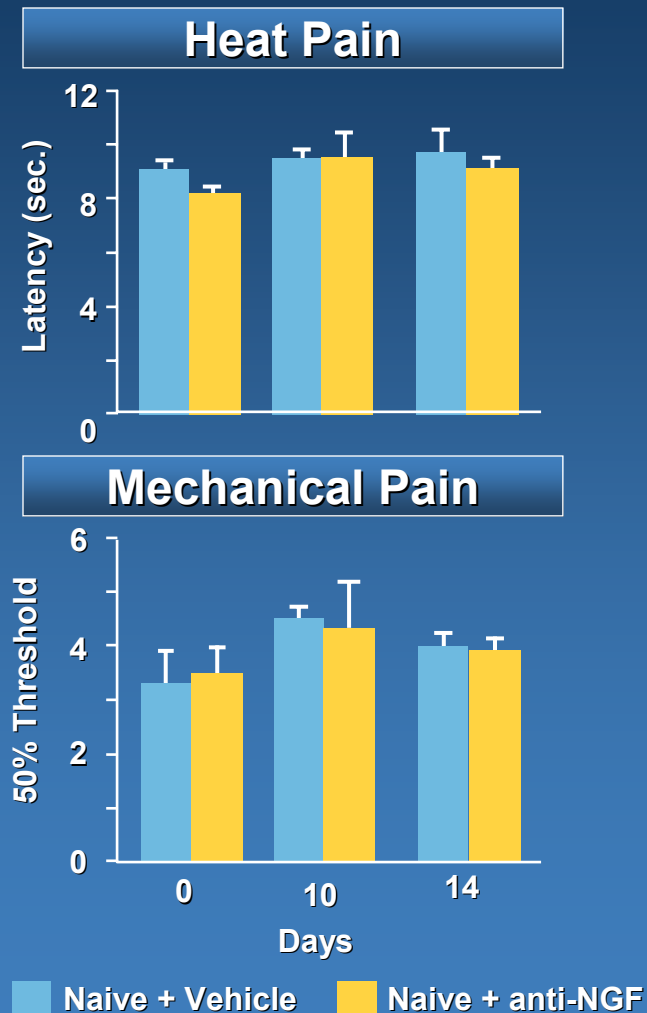


# NGF: Pain Signaling



- **NGF sensitizes TRPV1 ion channels**
  - Noxious heat/acidity (capsaicin receptor)
  - NGF causes phosphorylation of TRPV1 which leads to increased transport to cell surface and increased channel activity
- **NGF activates mast cells**
- **NGF triggers changes in gene expression**
  - Increases expression of proteins that further sensitize these neurons

# Anti-NGF Treatment Does Not Affect Acute Pain Sensation or Neuron Survival in Animals



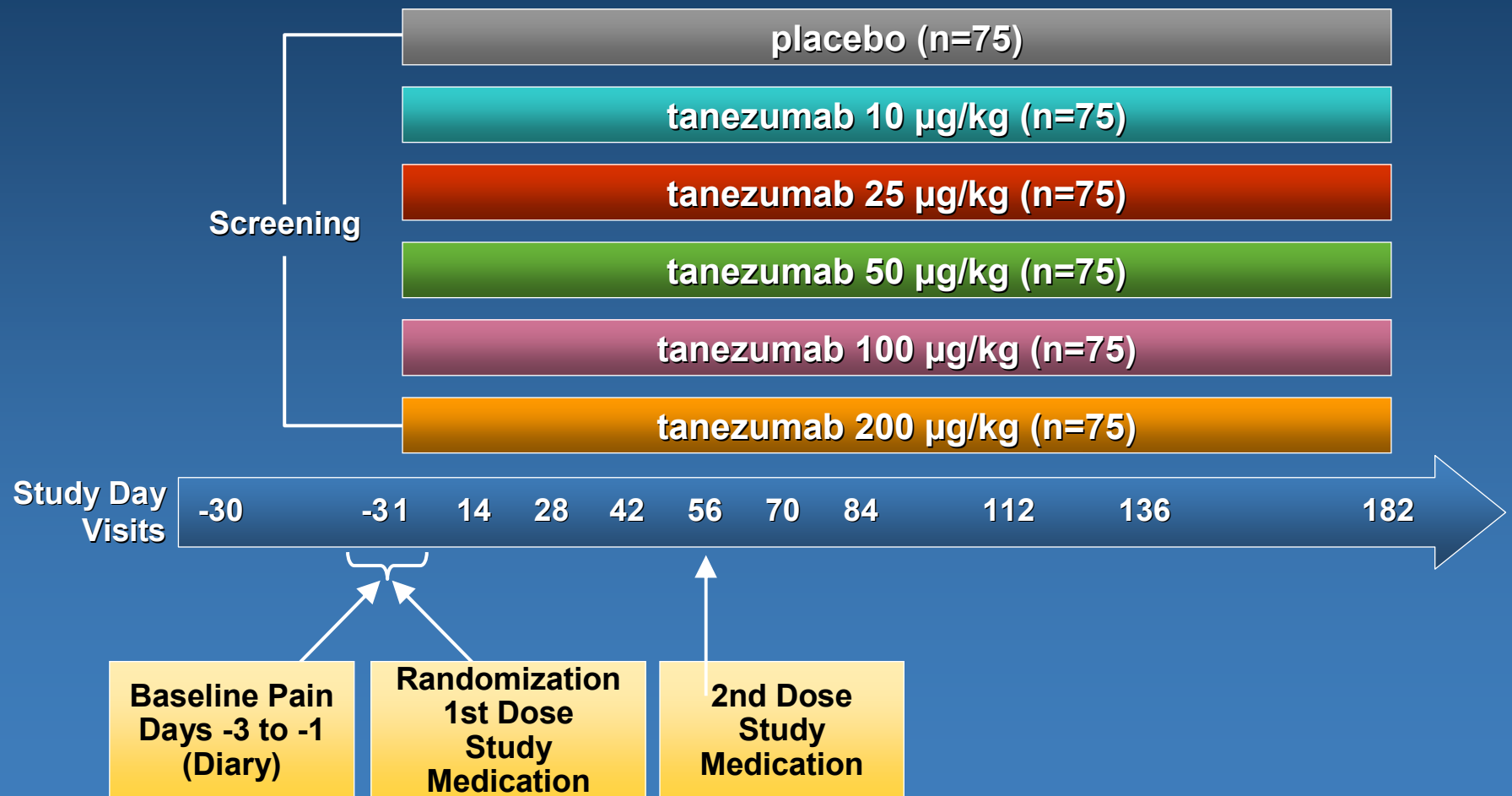
- 26-week study in adult cynomolgous monkeys with 0, 1, 10 & 30 mg/kg/week
  - No target organ toxicities
  - Extensive evaluation of nervous system

# Clinical Program Overview

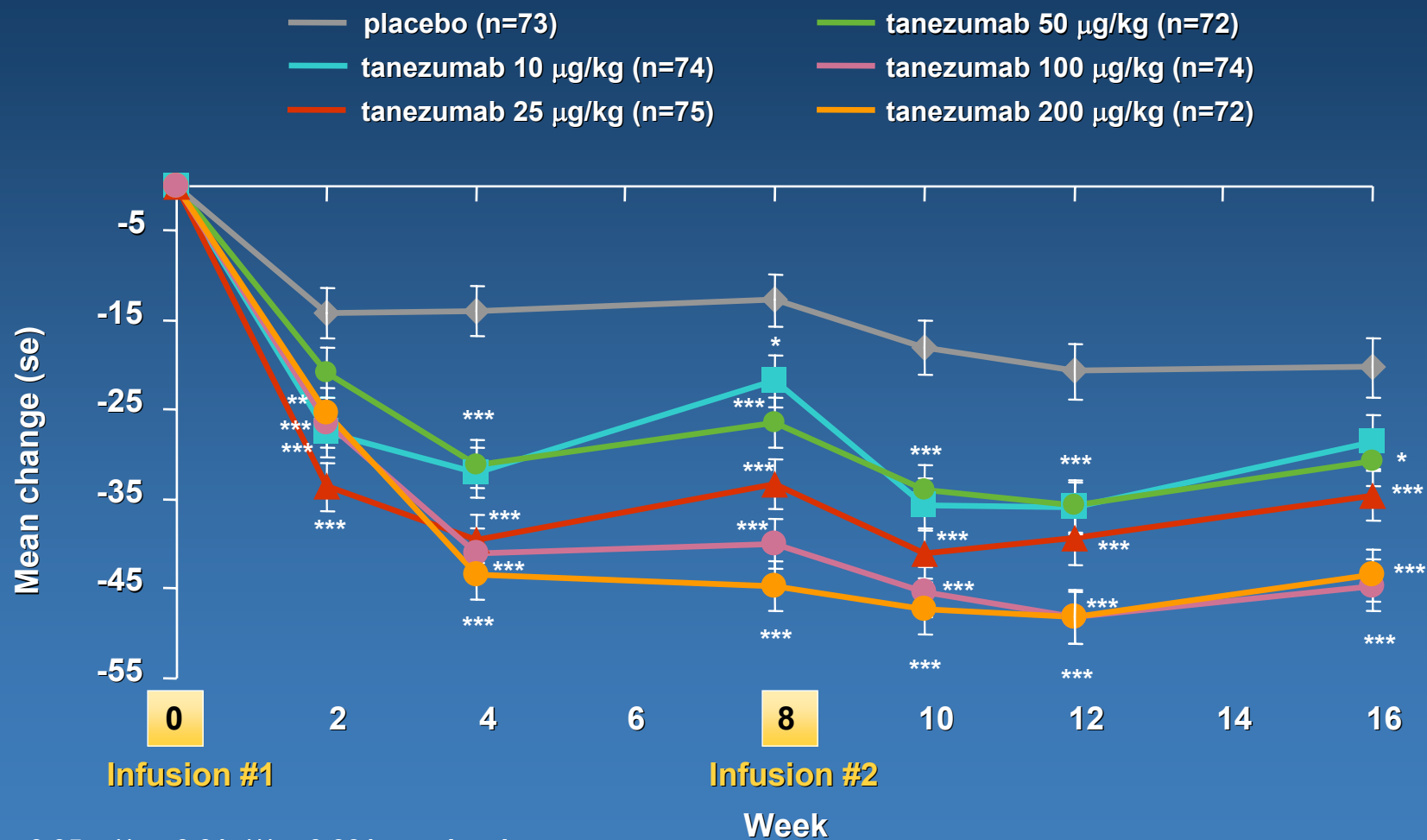
- **Exposure**
  - >675 patients treated with at least 1 dose
  - ~250 patients → 6 months treatment
  - ~60 patients → 12 months treatment
- **Osteoarthritis**
  - Phase 2 program complete
  - Encouraging open-label data ≤1 yr with 50 µg/kg IV q 8 wks
- **Phase 2 studies**
  - Chronic low back pain (CLBP) – completed
  - Neuropathic pain (PHN) – enrollment completed
  - Visceral pain
    - Interstitial cystitis – enrollment ongoing
    - Endometriosis (4Q), prostatitis (1Q)
  - Cancer Pain (metastatic bone pain – 1Q)
- **SC Route of administration**
  - IV/SC BE study (4Q)
- **RTU liquid formulation developed (refrigerated)**



# Dose-Ranging Knee OA Study 1008: Study Design



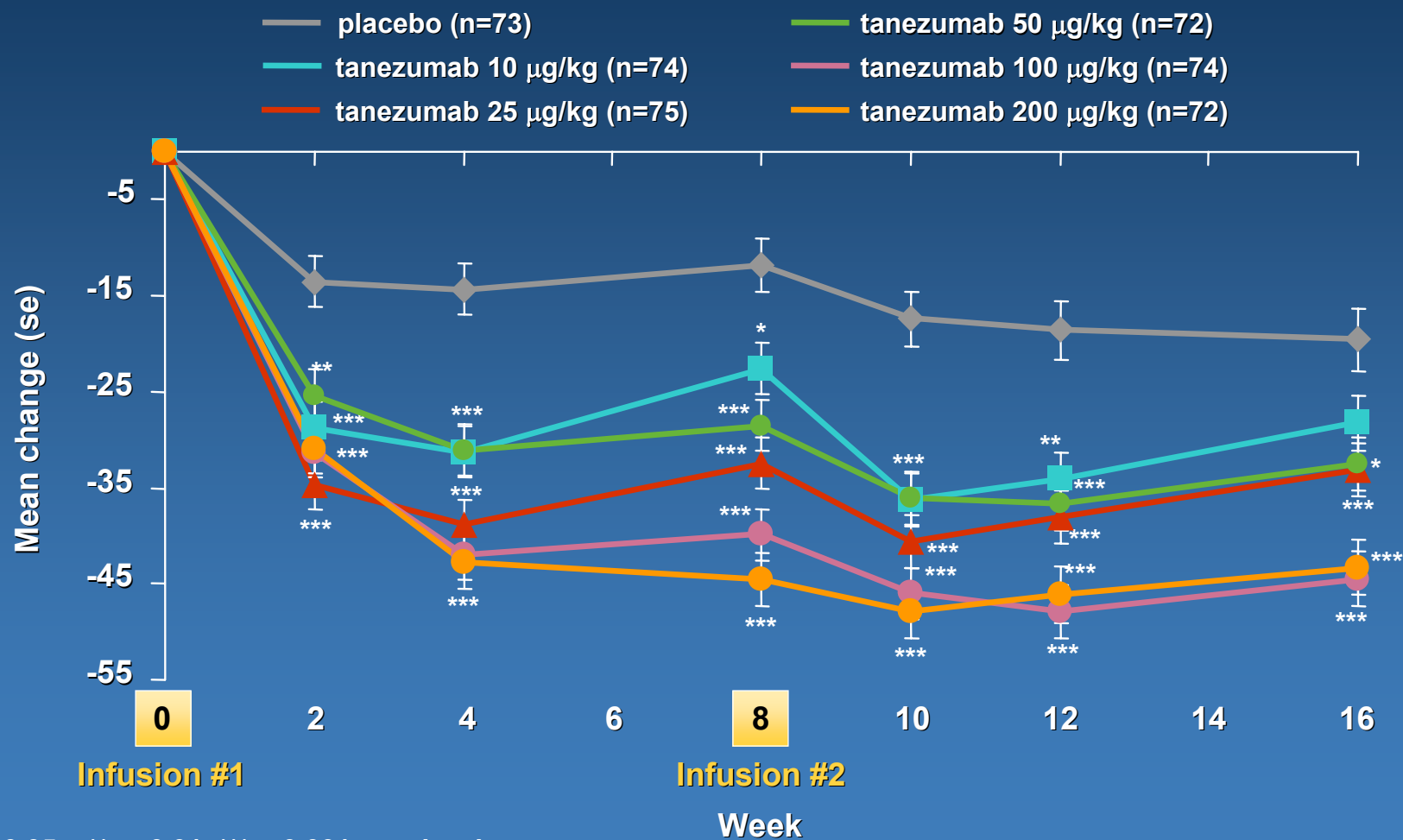
# WOMAC Pain Scale (VAS 0-100 mm)



\*p<0.05 \*\* p<0.01 \*\*\*p<0.001 vs. placebo  
 Baseline Scores = 62.1 – 69.2 mm



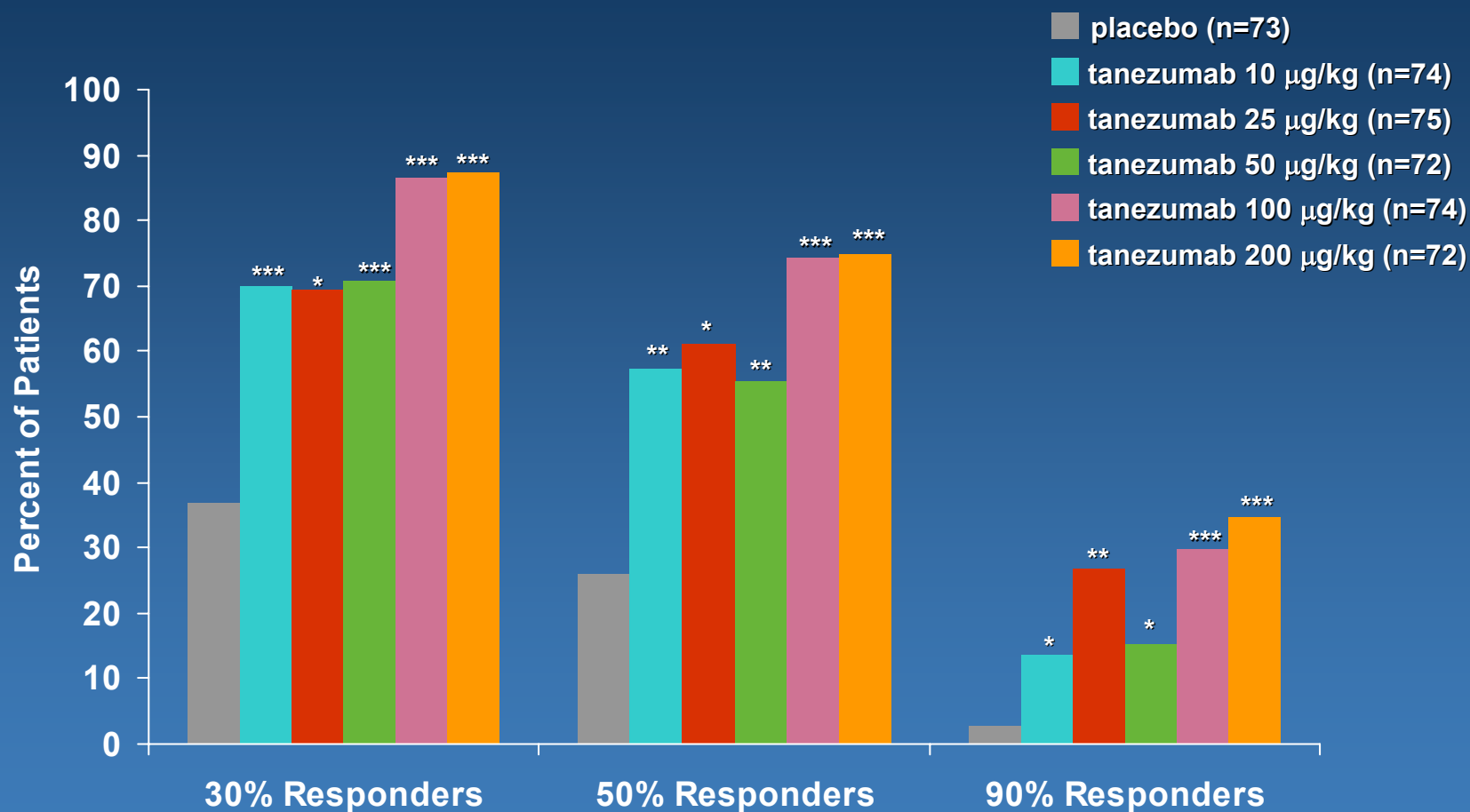
# WOMAC Function Scale (VAS 0-100 mm)



\*p≤0.05 \*\* p≤0.01 \*\*\*p≤0.001 vs. placebo  
 Baseline Scores = 62.1 – 69.2 mm



# Pain Responder Rates at Week 12

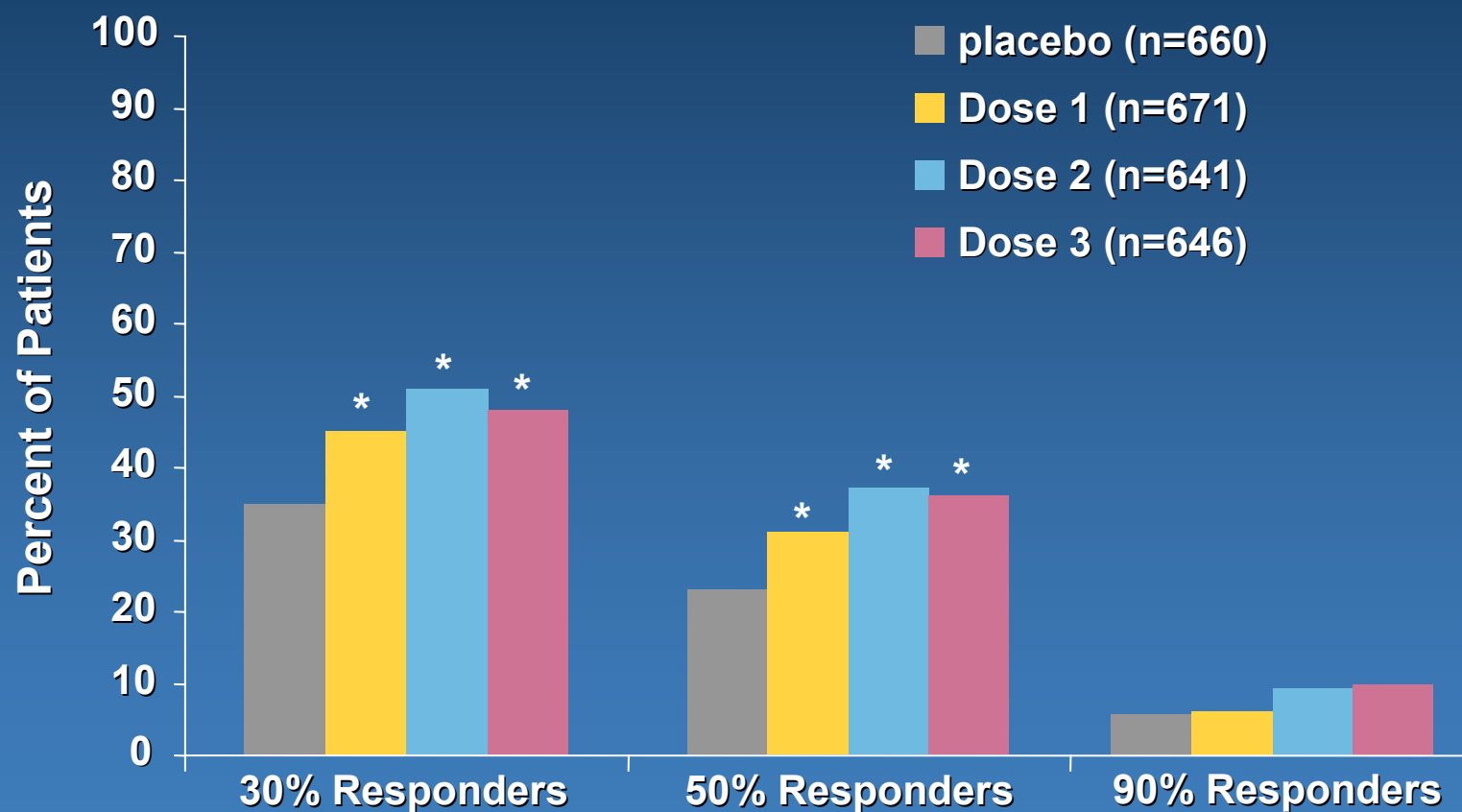


Active treatment group vs. placebo: \* $p \leq 0.05$  \*\*  $p \leq 0.01$  \*\*\* $p \leq 0.001$

Dworkin RH, Turk DC, Wywich KW, et al. Interpreting the clinical importance of treatment outcomes in chronic pain clinical trials: IMMPACT recommendations. *J Pain* 2008; 9: 105-121



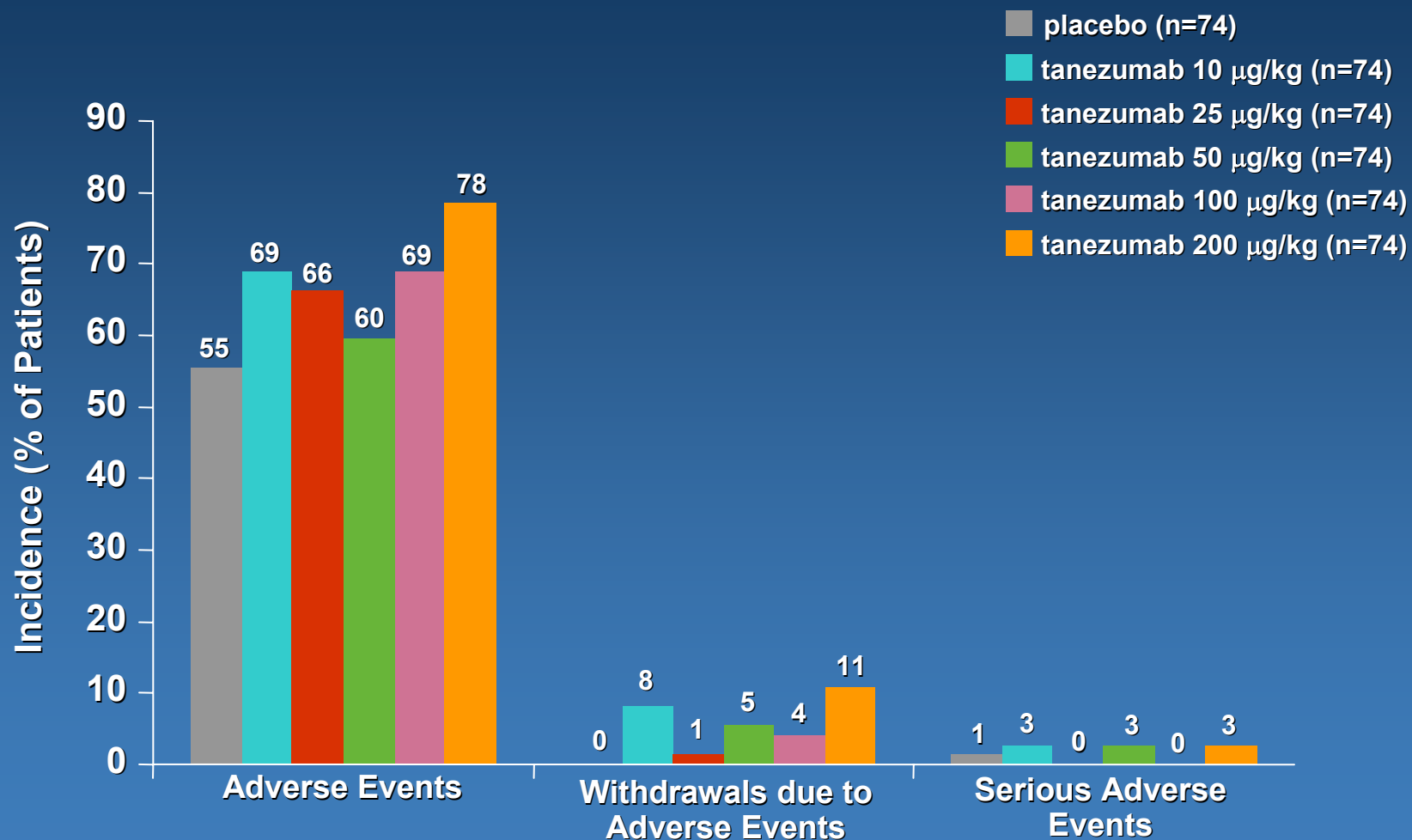
# Pain Responder Rates With an NSAID in Phase 3 OA Trials at Week 12



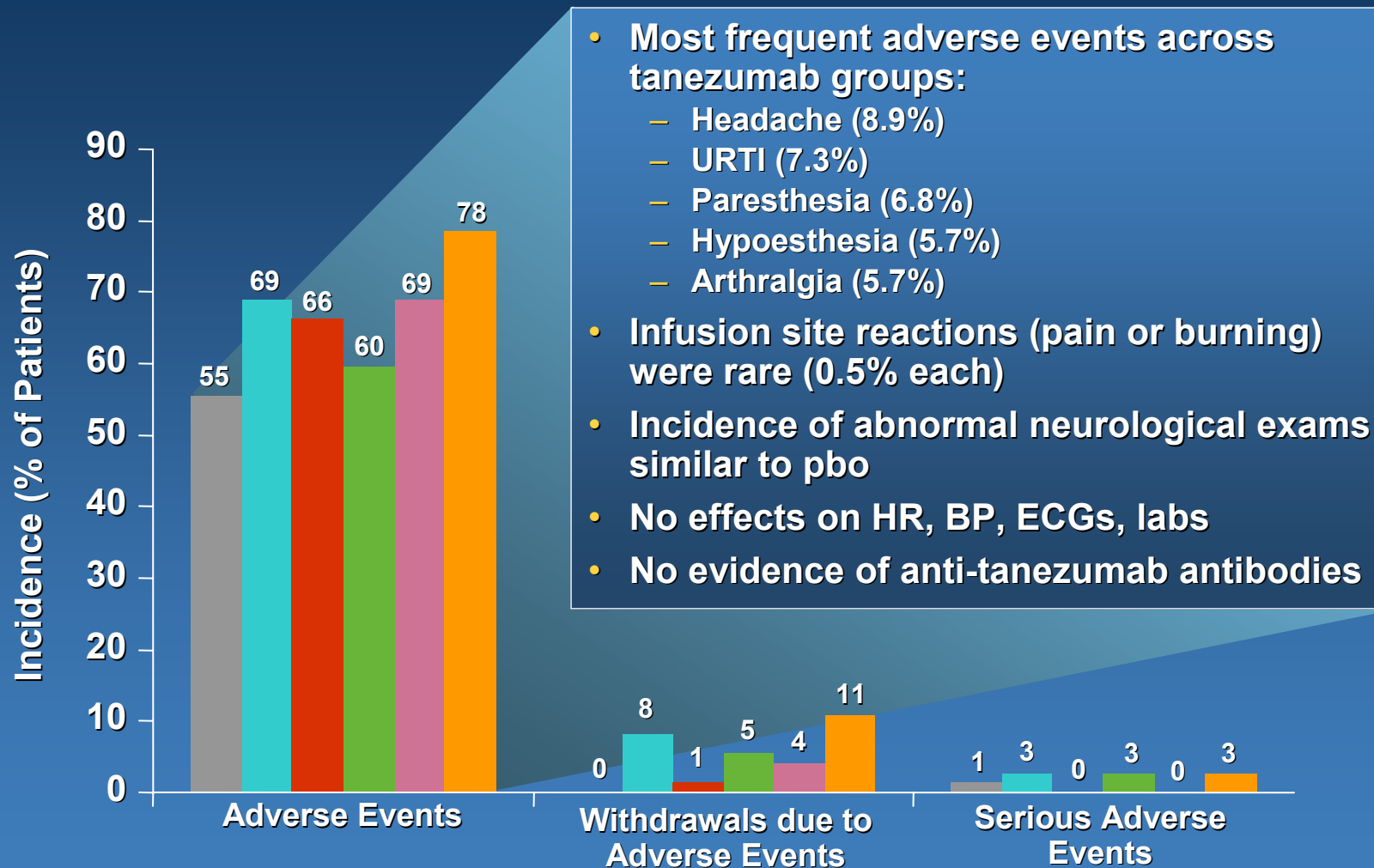
\*Active treatment group vs. placebo:  $p \leq 0.05$



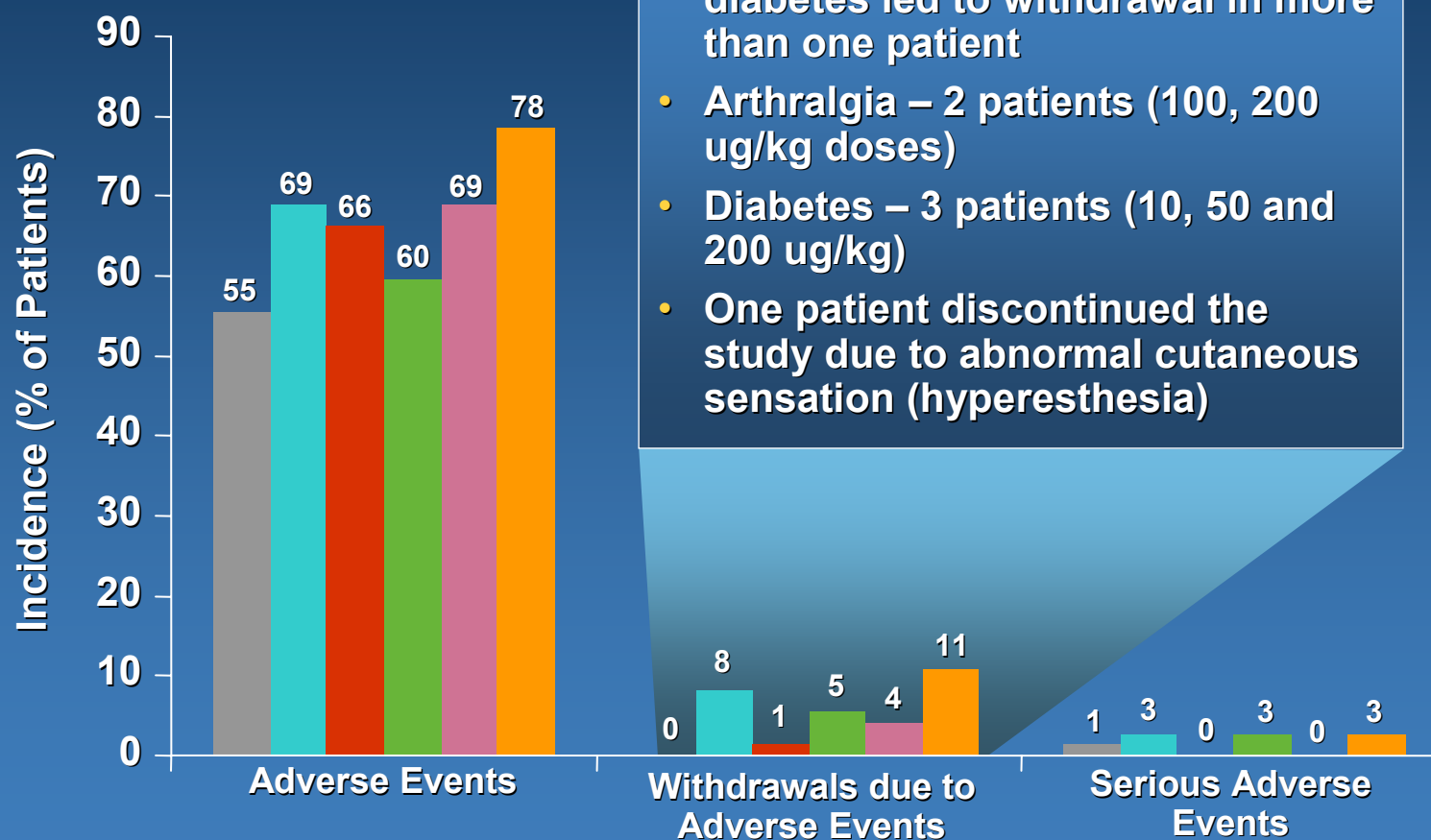
# Summary of Safety



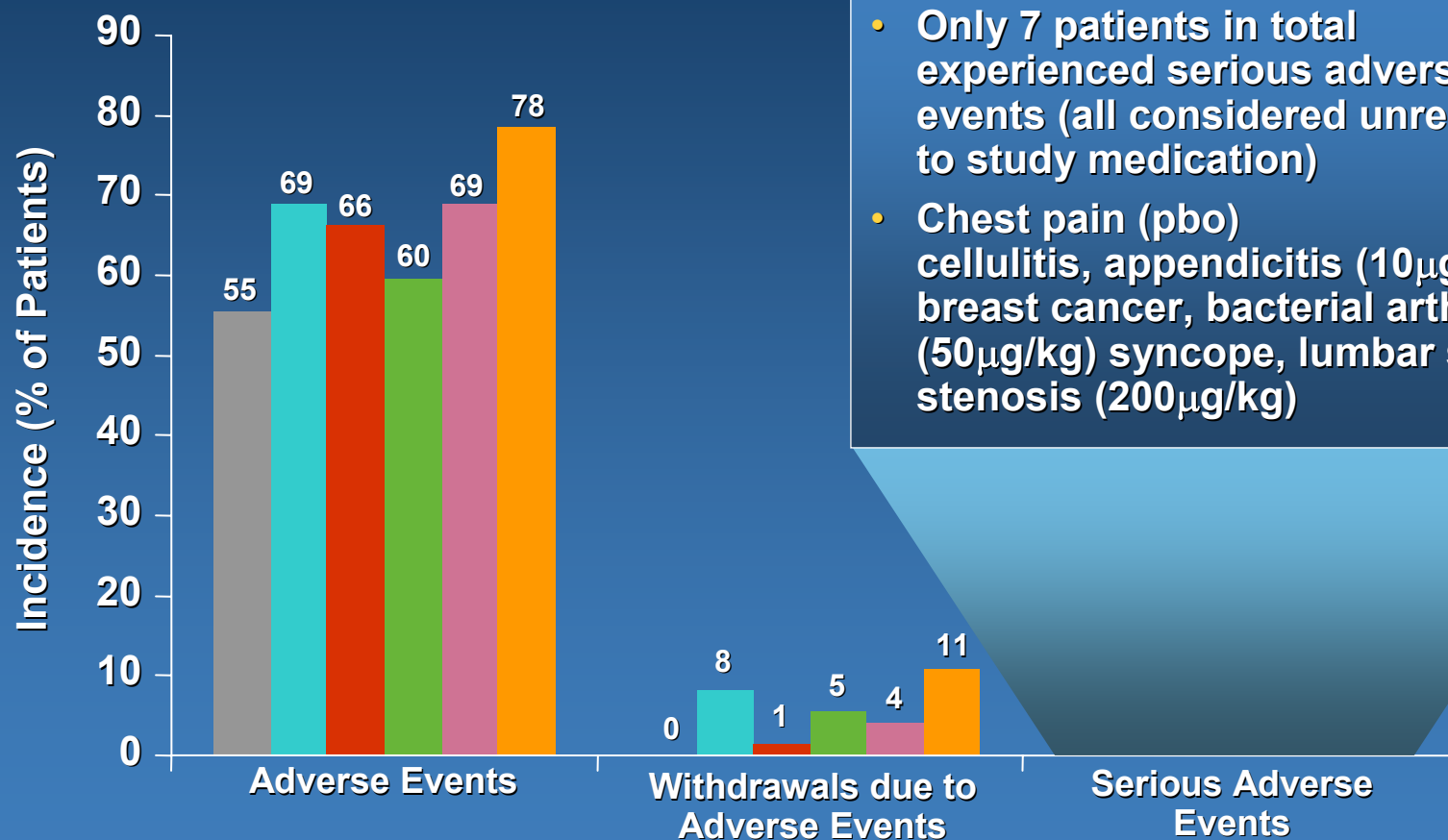
# Summary of Safety



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# Summary of Safety



- Only 7 patients in total experienced serious adverse events (all considered unrelated to study medication)
- Chest pain (pbo)  
cellulitis, appendicitis (10µg/kg)  
breast cancer, bacterial arthritis (50µg/kg)  
syncope, lumbar spine stenosis (200µg/kg)



# Adverse Events Related to Abnormal Peripheral Sensation

- **Allodynia**
  - Clothing/touch evoke pain sensation
- **Dysesthesia:**
  - Sensitivity to touch and clothing
  - Sunburn/hot sensation
- **Paresthesia**
  - Tingling, pricking, or pins & needles sensation
- **Hyperesthesia (Hypoesthesia)**
  - High (low) sensitivity to touch, pain, or other sensory stimuli

# Adverse Events Related to Abnormal Peripheral Sensation

n (%)	placebo N=74	tanezumab (µg/kg)					Combined N=370
		10 N=74	25 N=74	50 N=74	100 N=74	200 N=74	
Any AE	2 (2.7)	4 (5.4)	4 (5.4)	4 (5.4)	13 (17.6)	12 (16.2)	37 (10.0)
Allodynia	0	0	0	0	1 (1.4)	1 (1.4)	2 (0.5)
Dysesthesia	0	0	0	0	1 (1.4)	1 (1.4)	2 (0.5)
Hyperesthesia	0	0	0	3 (4.1)	4 (5.4)	4 (5.4)	11 (3.0)
Paresthesia	2 (2.7)	4 (5.4)	4 (5.4)	1 (1.4)	8 (10.8)	8 (10.8)	25 (6.8)
Hypoesthesia	0	1 (1.4)	7 (9.5)	2 (2.7)	5 (6.8)	6 (8.1)	21 (5.7)

**Early, Transient, Mild-to-Moderate, Normal/Minor Changes on Neurological Exams; Not Consistent with Structural Damage**



# Tanezumab: Summary

- Therapeutic potential in a number of pain conditions
- Fixed low doses administered 6 times per year
- Encouraging safety profile to date
- Dose-related transient abnormal cutaneous sensations have been observed – not treatment limiting
- Long-term effects on sensory and autonomic function to be investigated in Phase 3
  - Large safety database
  - Neurological Impairment Score
  - Routine neurological exams
  - Nerve conduction velocity assessment
  - Autonomic function testing
  - Cutaneous peripheral nerve density
- Upcoming milestones



**Management of Fibromyalgia  
with Esreboxetine**

# Fibromyalgia: Clinical Characteristics

- A syndrome characterized by:
  - Widespread soft tissue and muscular pain
  - Decreased pain threshold (tenderpoints)
  - Fatigue: 81% – “usually or always too tired”<sup>1</sup>
  - Disturbed sleep: 75% consider their sleep nonrestorative<sup>1</sup>
  - Anxiety or depression
  - IBS, Raynaud’s, headache, paresthesias
- Prevalence 2.0% (U.S.); 3–6 million people
  - Diagnosed ~1 million
  - 3.4% for women, 0.5% for men
  - Most common in women ages ≥50 years
- Difficult condition for patients – diagnosis and treatment

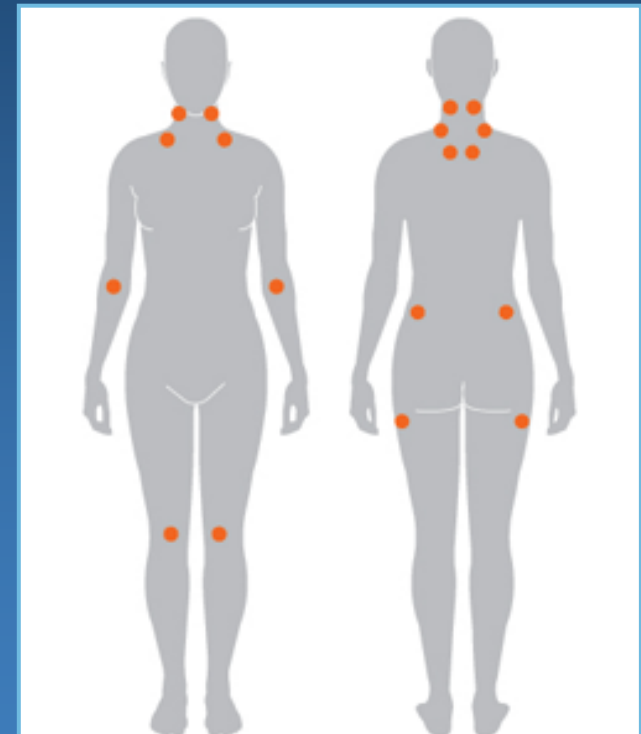
<sup>1</sup> Wolfe et al. *Arthritis Rheum* 1990

<sup>2</sup> Hudson et al. *Rheumatic Dis Clin N A* 1996

<sup>3</sup> Dwight et al. *Psychosomatics* 1998

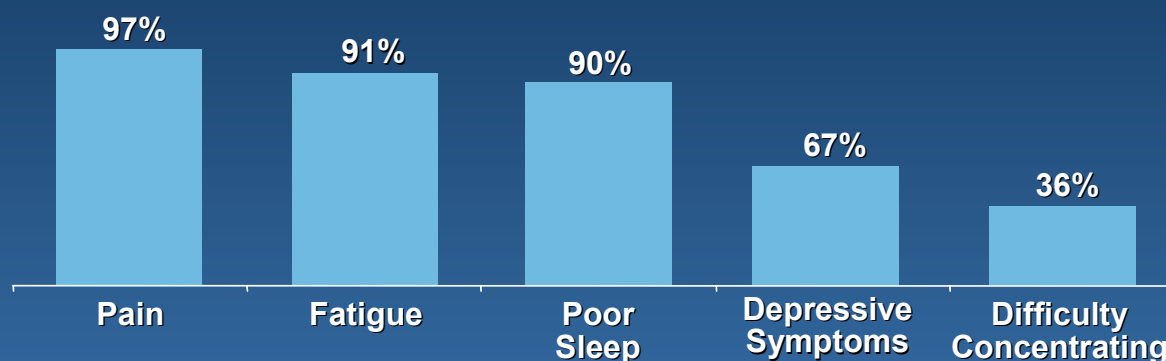
<sup>4</sup> Epstein et al. *Psychosomatics* 1999

Fibromyalgia Tender Points



# Esreboxetine: Unmet Patient Needs

## % of Fibromyalgia Patients with Symptoms\*



## Key Value Drivers

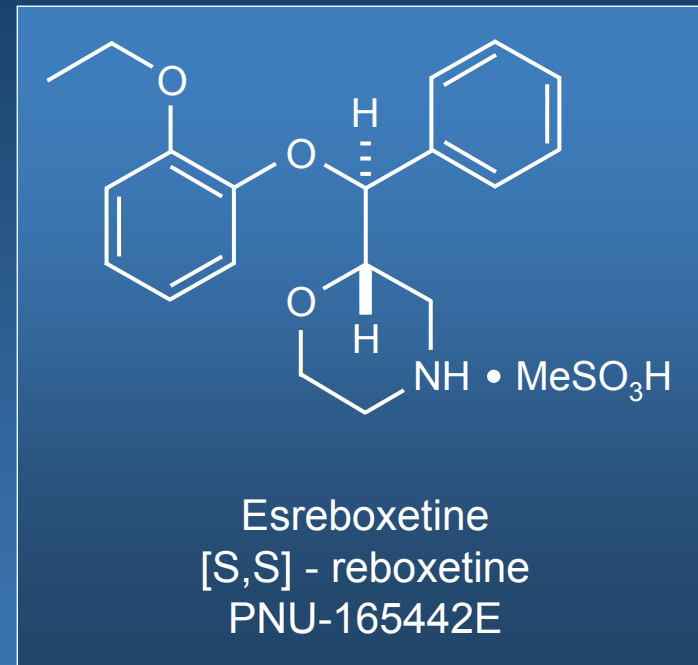
	Widespread Pain	Fatigue	Poor Sleep	Function	Difficulty Concentrating	Depression
Lyrica	✓	Unmet Need Gap		✓	Unmet Need Gap	
duloxetine	✓	Unmet Need Gap		✓	Unmet Need Gap	✓
milnacipran	✓	Unmet Need Gap		✓	Unmet Need Gap	✓
esreboxetine	✓	✓		✓	✓	✓

Pfizer Internal Marketing Research Data, 2008



# Esreboxetine

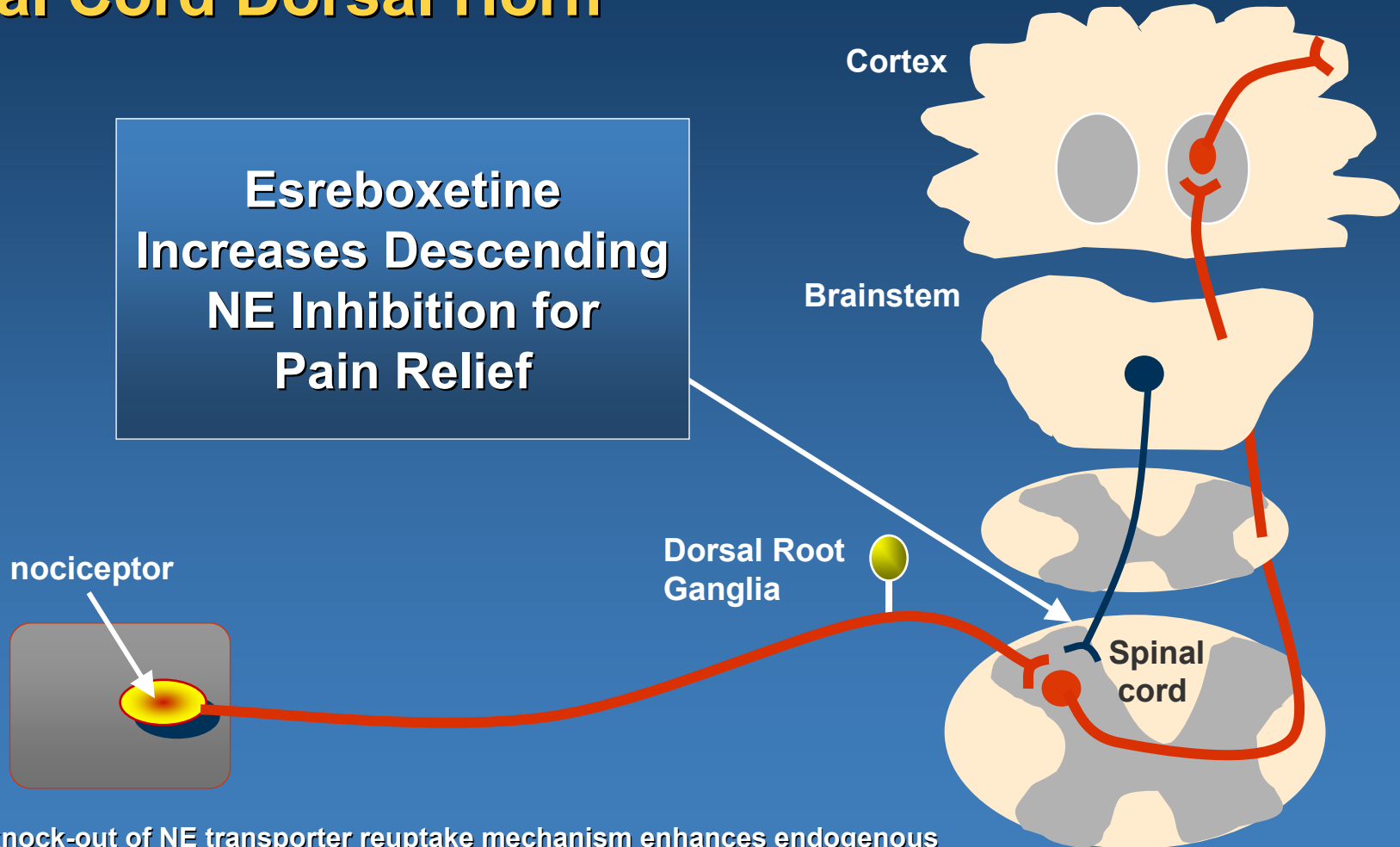
- Selective norepinephrine reuptake inhibitor (NRI)
- More selective isomer of Edronax (racemic reboxetine)
  - Approved for depression in over 40 countries outside the US
- Different pharmacologic approach than Lyrica
- Once daily administration
- In Phase 3 development for fibromyalgia



NET:SERT selectivity  
Esreboxetine >>>racemic reboxetine>>milnacipran>duloxetine>fluoxetine

# Putative Site and Mechanism of Action: Enhancing Norepinephrine (NE) Transmission at Spinal Cord Dorsal Horn

Esreboxetine  
Increases Descending  
NE Inhibition for  
Pain Relief

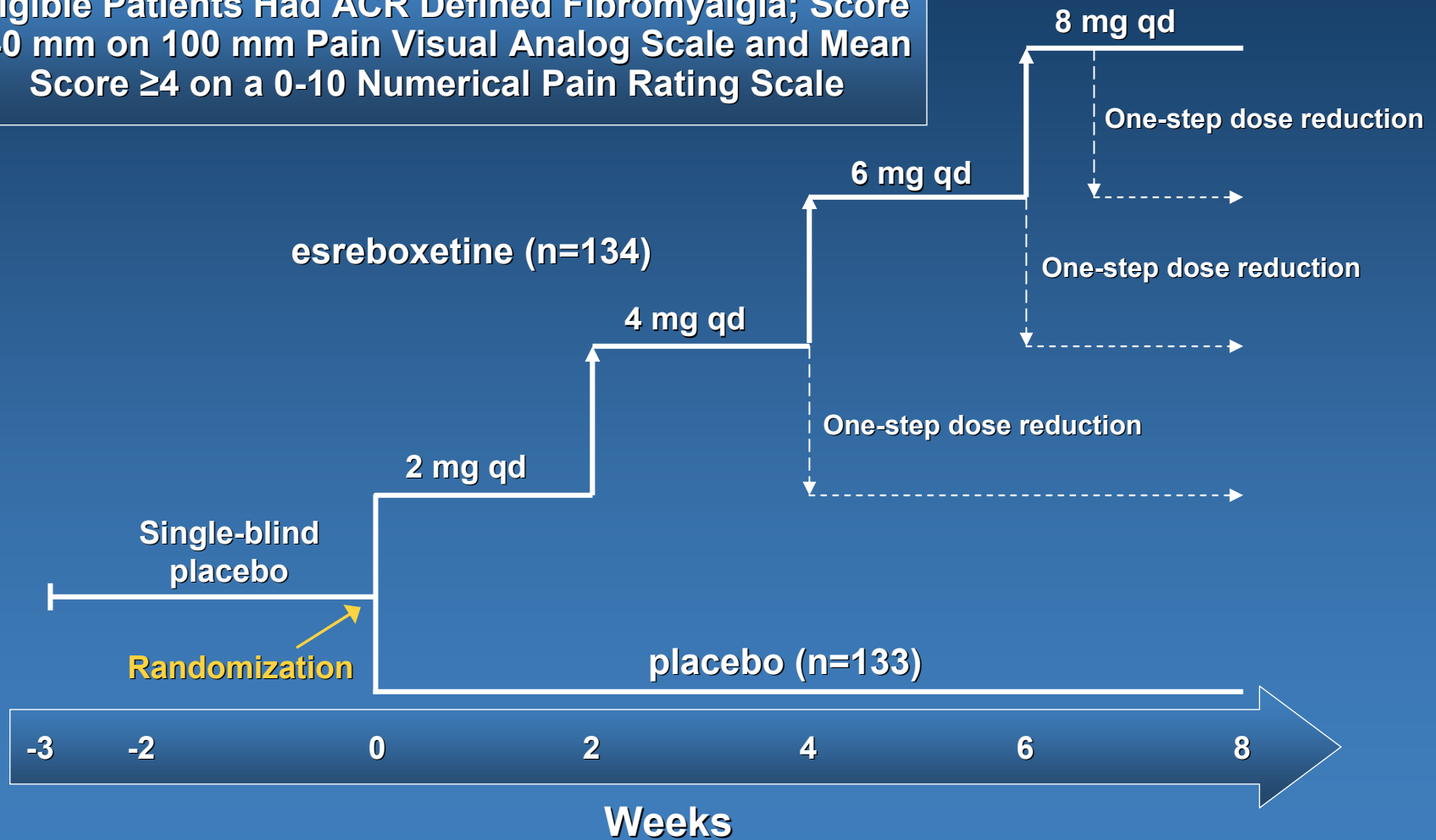


Specific knock-out of NE transporter reuptake mechanism enhances endogenous and exogenous opioid analgesia (Bohn et al., *J. Neurosci.*, 20: 9040, 2000)



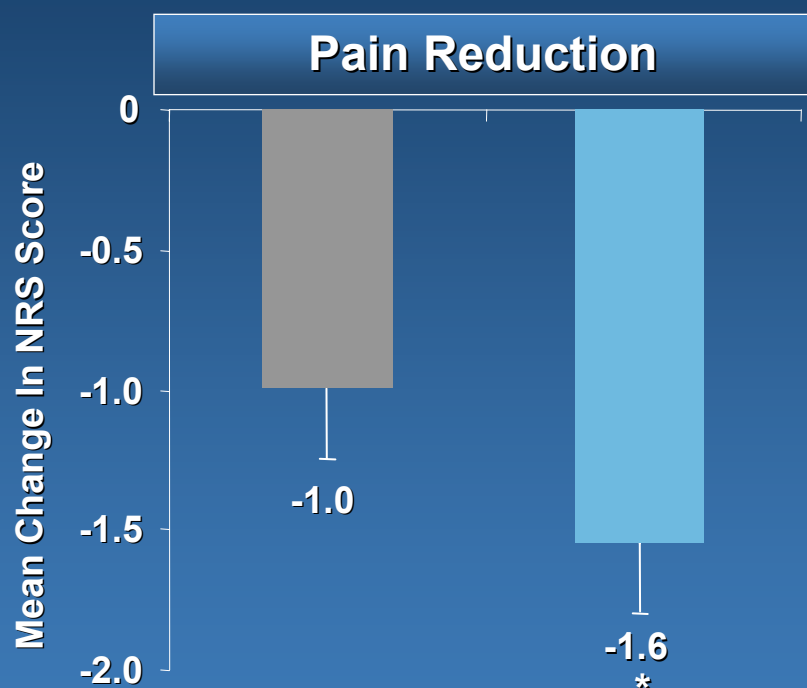
# Phase 2 Study Design: Study 1034

Eligible Patients Had ACR Defined Fibromyalgia; Score  $\geq 40$  mm on 100 mm Pain Visual Analog Scale and Mean Score  $\geq 4$  on a 0-10 Numerical Pain Rating Scale

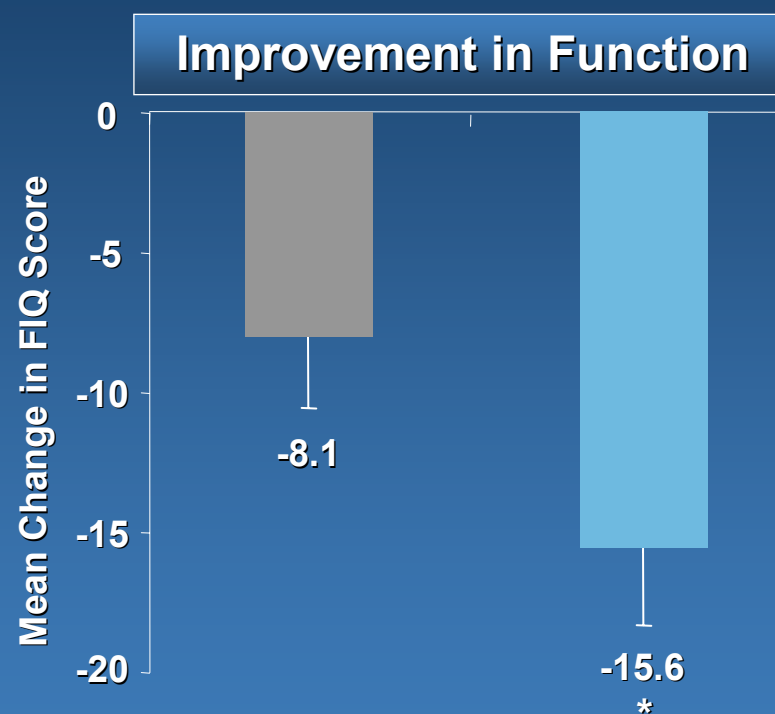


# Efficacy in Fibromyalgia

■ placebo (n=133)  
■ esreboxetine (n=134)



Scale 0 (no pain) to 10 (worst pain)  
Baseline Scores: 6.8 (both groups)



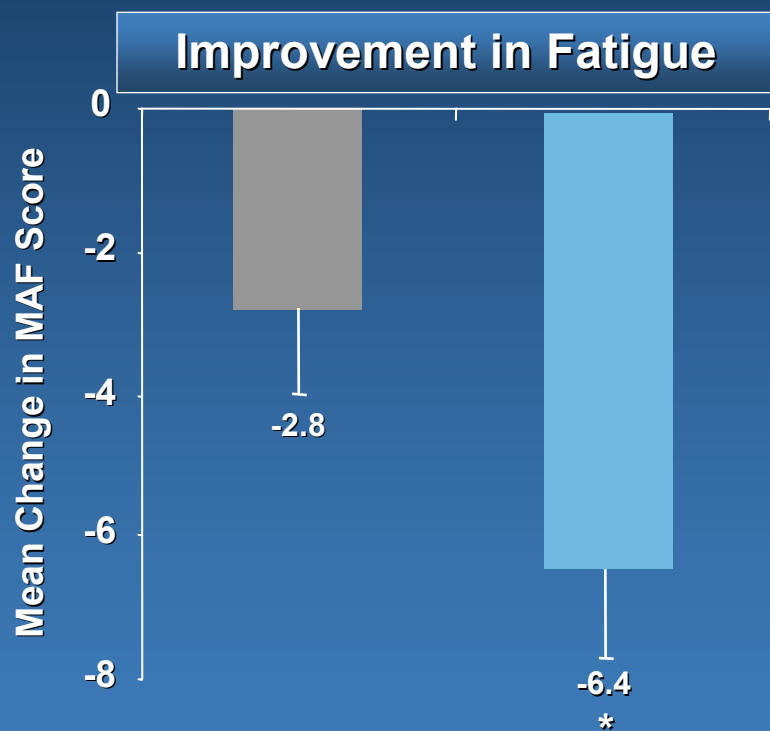
Scale 0 (none) to 100 (max impairment)  
Baseline Scores: 62.8 (placebo)  
61.4 (esreboxetine)

\*p<0.01 vs. placebo

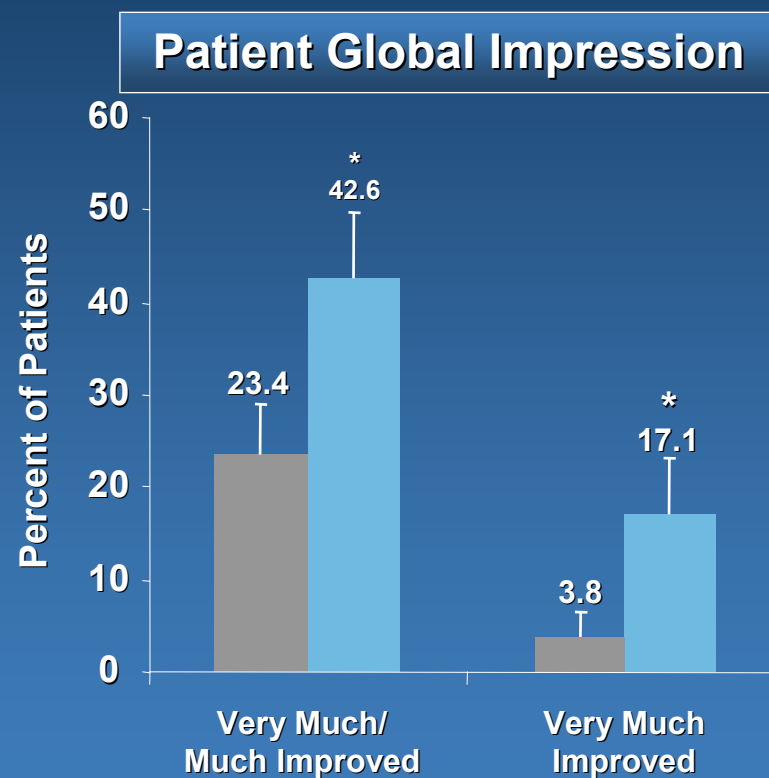


# Efficacy in Fibromyalgia

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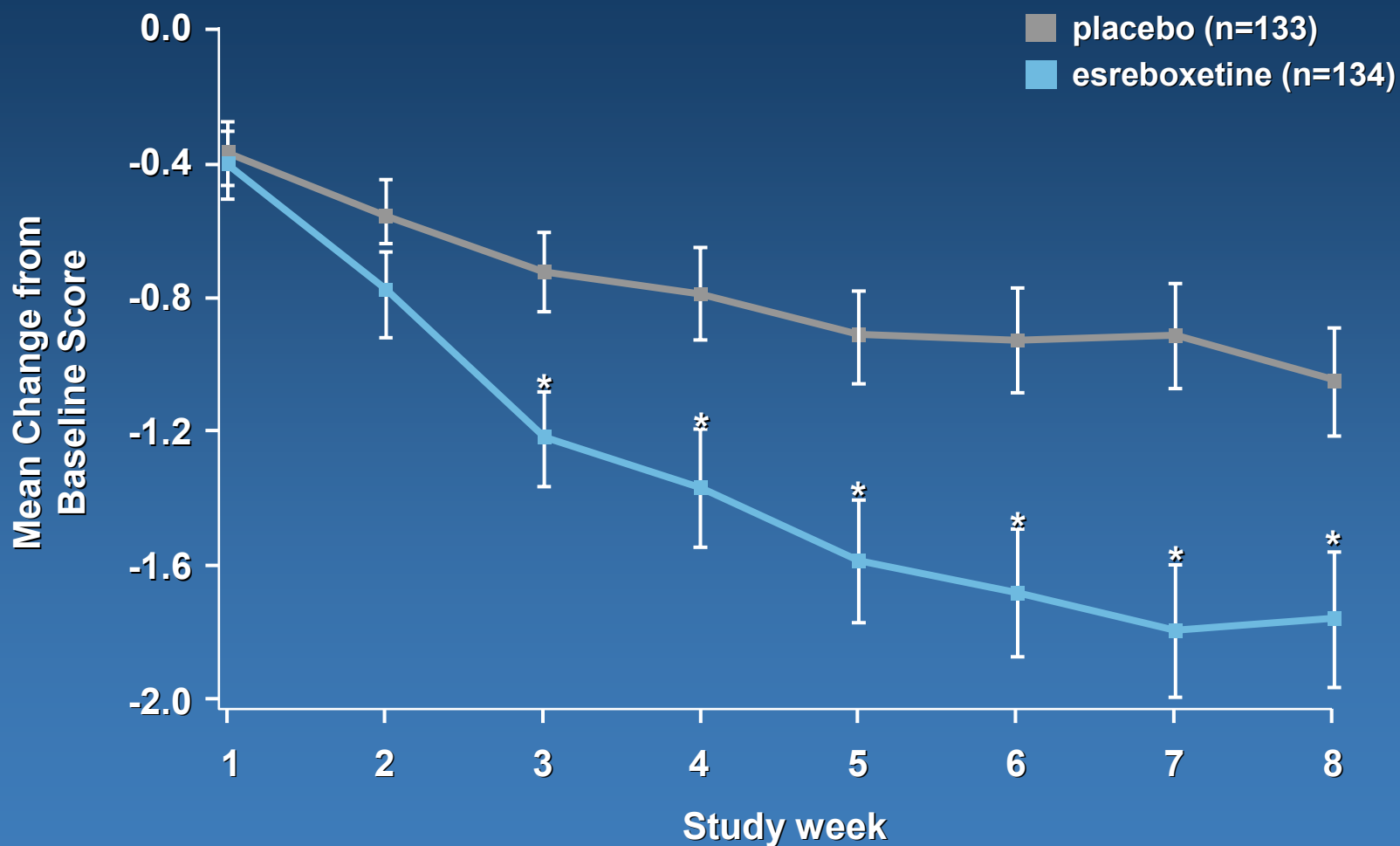
Scale 0 (none) to 50 (maximum)  
Baseline Scores: 37.8 (placebo)  
37.6 (esreboxetine)



\*p<0.01 vs. placebo



# Time Course of Pain Relief

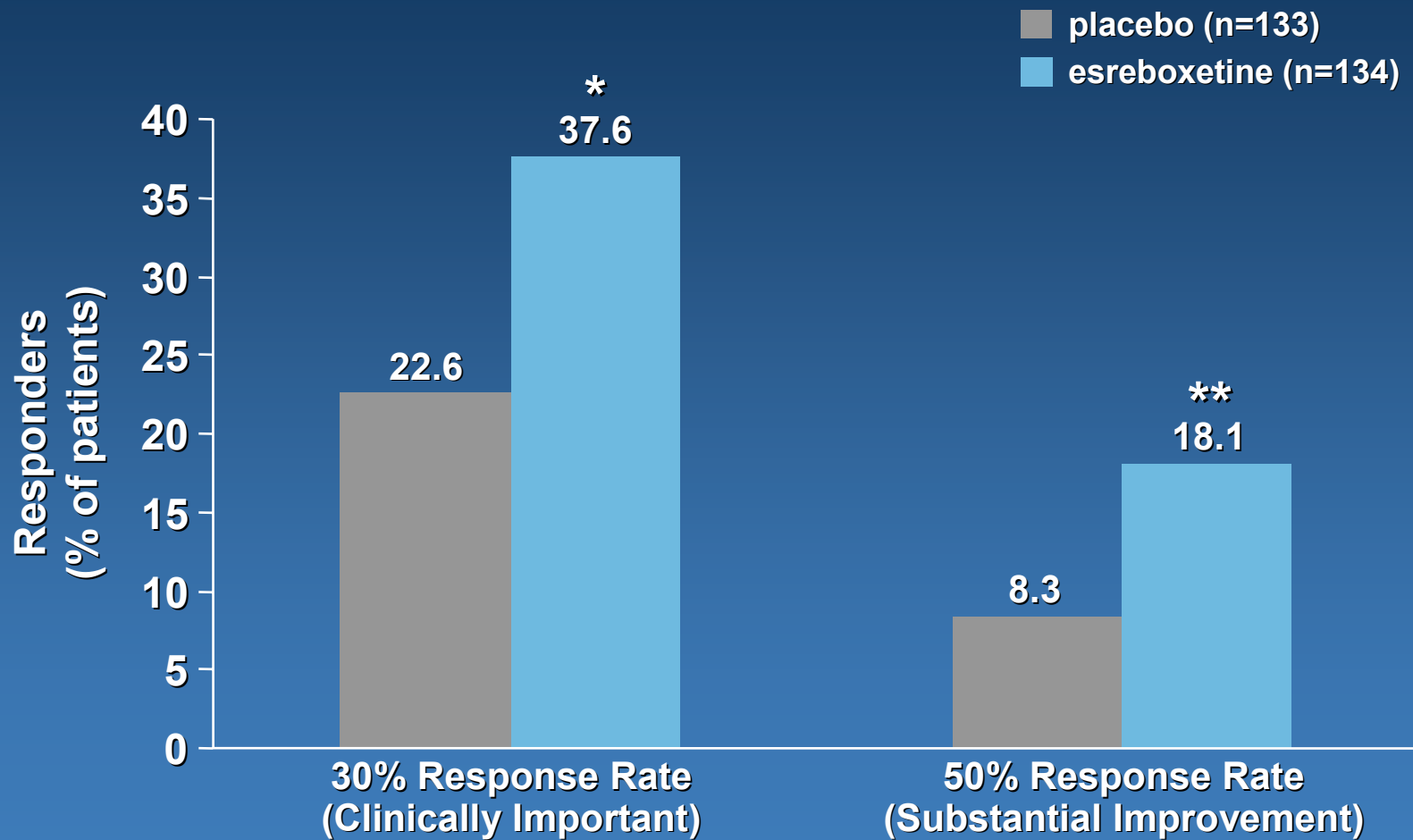


\* p<0.05 vs. placebo

Mean (SD) Baseline Score; placebo = 6.8 (1.4); esreboxetine = 6.8 (1.4)



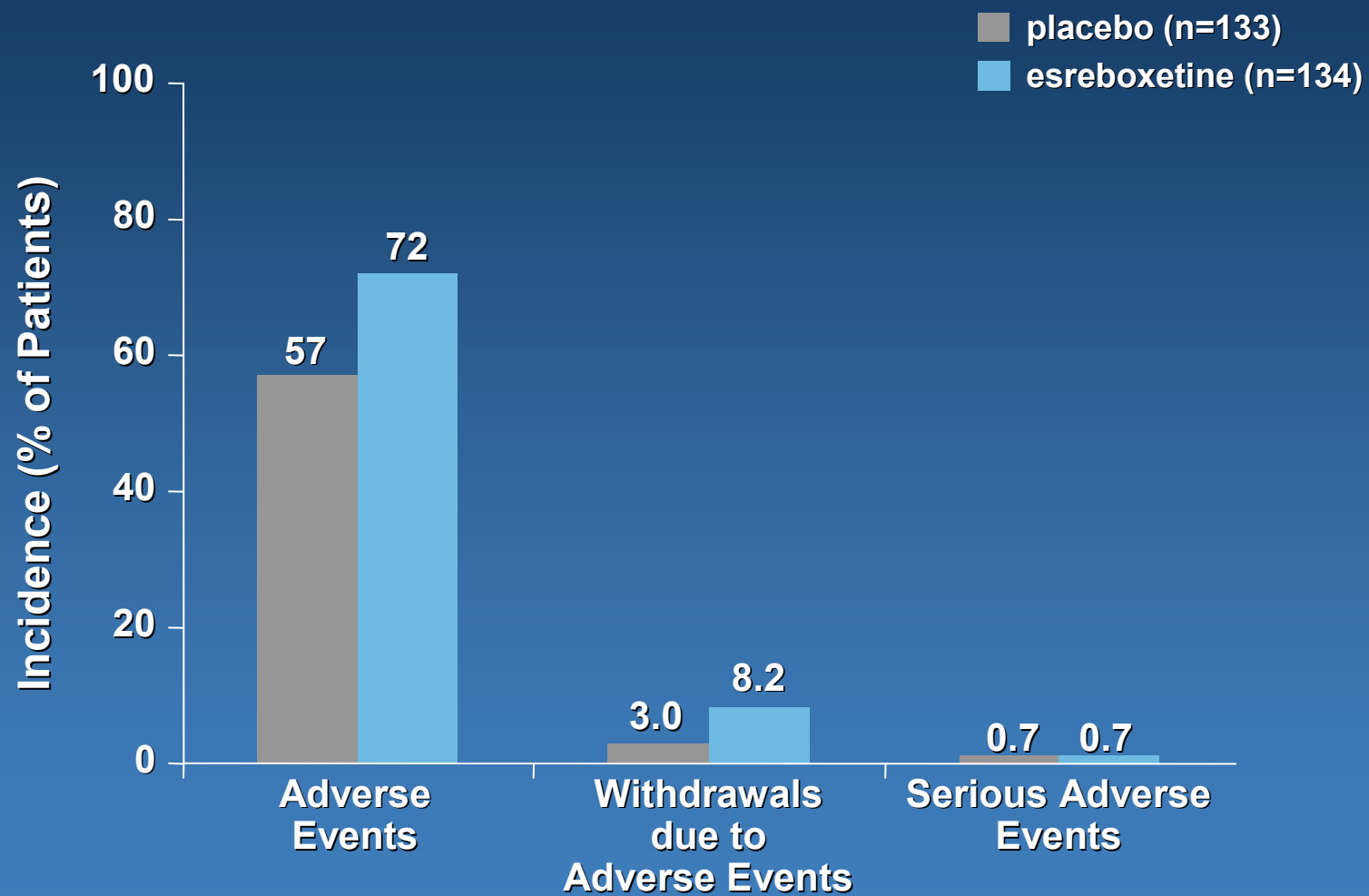
# Responder Rates: Reductions in Pain



\*p=0.004; \*\*p=0.01 vs. placebo



# Summary of Safety



# Incidence of Adverse Events ( $\geq 5\%$ )

	placebo (n=133) n (%)	esreboxetine (n=134) n (%)
Constipation	7 (5.3)	26 (19.4)
Insomnia	5 (3.8)	24 (17.9)
Dry mouth	3 (2.3)	22 (16.4)
Headache	5 (3.8)	19 (14.2)
Nausea	4 (3.0)	12 (9.0)
URTI	7 (5.3)	6 (4.5)
Dizziness	2 (1.5)	9 (6.7)
Nasopharyngitis	6 (4.5)	5 (3.7)
Fatigue	6 (4.5)	2 (1.5)
Hyperhidrosis	2 (1.5)	7 (5.2)
Palpitations	2 (1.5)	6 (4.5)

# Effects on Blood Pressure and Heart Rate

Parameter	placebo (n=133)		esreboxetine (n=134)	
	Baseline Mean (SD)	At 8 weeks Mean (SD)	Baseline Mean (SD)	At 8 weeks Mean (SD)
Systolic BP (mmHg)	123.6 (13.7)	123.8 (14.1)	120.6 (14.4)	120.9 (14.5)
Diastolic BP (mmHg)	77.0 (8.5)	76.7 (9.1)	76.3 (8.4)	77.7 (8.6)
Sitting heart rate (bpm)	74.1 (9.4)	75.5 (9.7)	73.2 (9.8)	81.6 (10.7)

- No clinically relevant difference in systolic or diastolic BP was observed between esreboxetine and placebo
- Esreboxetine-treated exhibited a mean increase in heart rate of 8 bpm

# Esreboxetine: Summary

- **Therapeutic potential in fibromyalgia**
  - Pain, function, fatigue and cognition
  - Potential for study with Lyrica
  - Differentiation from mixed reuptake inhibitors
  - Benefit: risk optimized in phenotypic subgroups
- **Encouraging safety profile to date**
  - Differentiation from mixed reuptake inhibitors
- **Mechanism-based safety and tolerability to be investigated in Phase 3**
  - Cardiovascular safety
  - Anticholinergic-like effects: constipation, urinary retention
- **Upcoming milestones**



## **CP-690,550 Update**

*Ethan Weiner, M.D.*

*Development Head for Inflammation Therapeutics*

*October 28, 2008*

# CP-690,550 Update

- **Significant Unmet Need**
- **Mechanism of Action**
- **Review of Program and Previous RA Data**
- **New Presentations at ACR**
  - 12 week dose response data (study 1025)
  - Open Label Extension (study 1024)
  - MTX DDI Study (study 1013)
- **Summary**

# CP-690,550 Update

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# Unmet Need in RA Market

- **Limitations of current products**
- **Needs of physicians and patients**
- **A significant need exists for new oral treatments beyond the treatments of the last three decades**

## **CP-690,550 – A Exciting Potential New Development in the Treatment of RA**

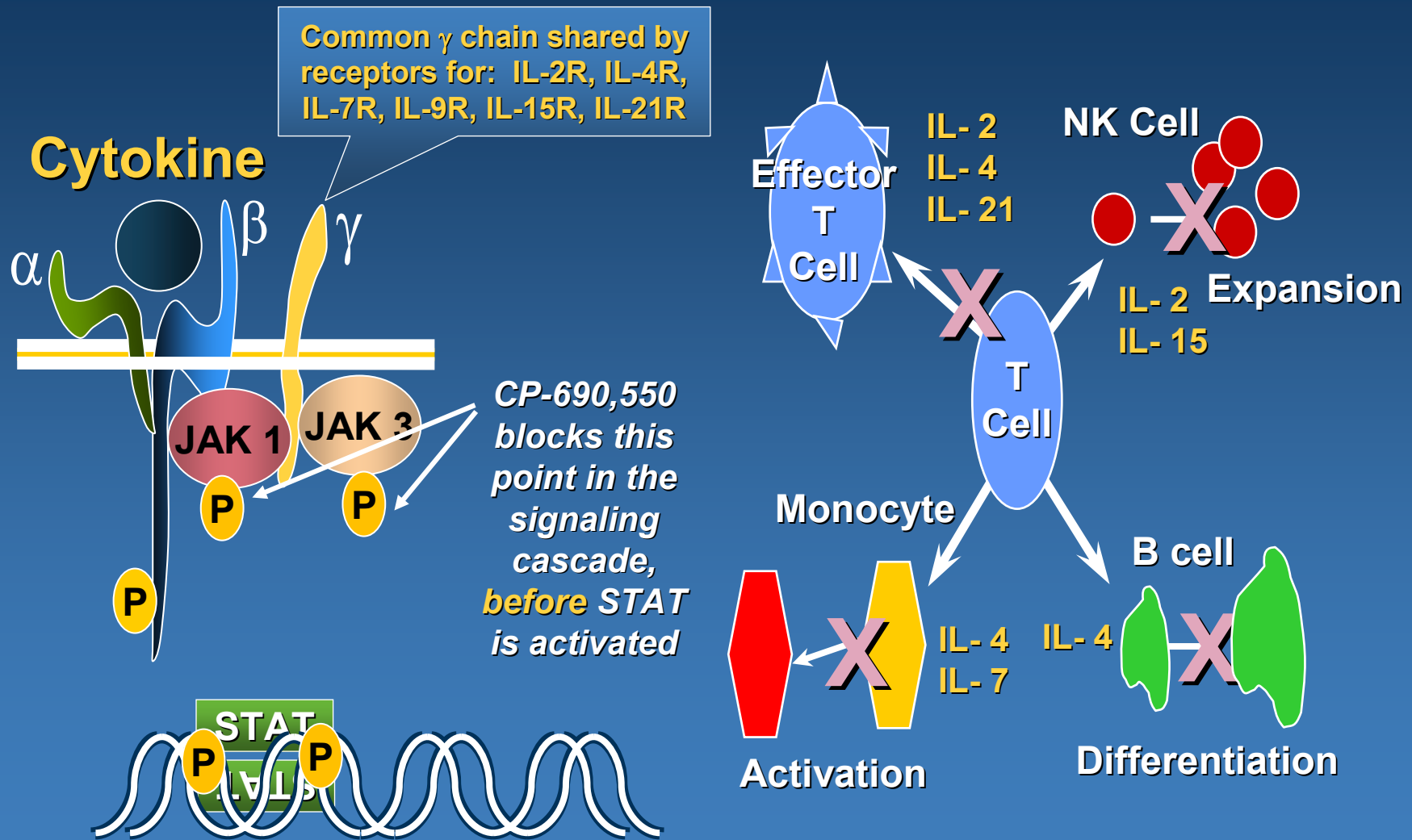
- **If successful, CP-690,550 could be the first new oral DMARD to be marketed in more than 10 years**
- **CP-690,550 is the first Janus Kinase inhibitor, a novel immune pathway mechanism that has the potential to treat patients afflicted by a number of autoimmune diseases**
- **A significant need exists for new treatments beyond the current paradigm of methotrexate (and other older DMARDs), and injectable TNF inhibitors**



# CP-690,550 Update

- Significant Unmet Need
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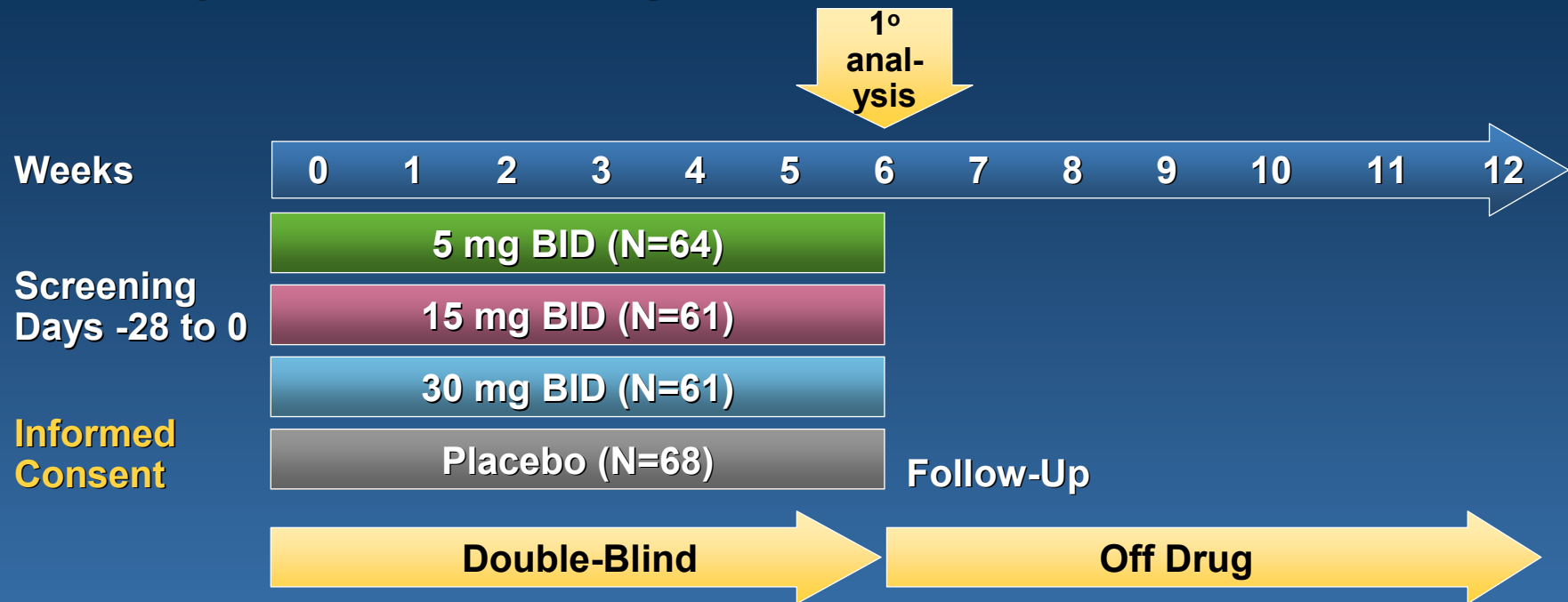
# Cytokine Signaling of JAK



# CP-690,550 Update

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- Mechanism of Action
- Review of Program and Previous RA Data
- New Presentations at ACR
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  - Open Label Extension (study 1024)
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# Study 1019: Design



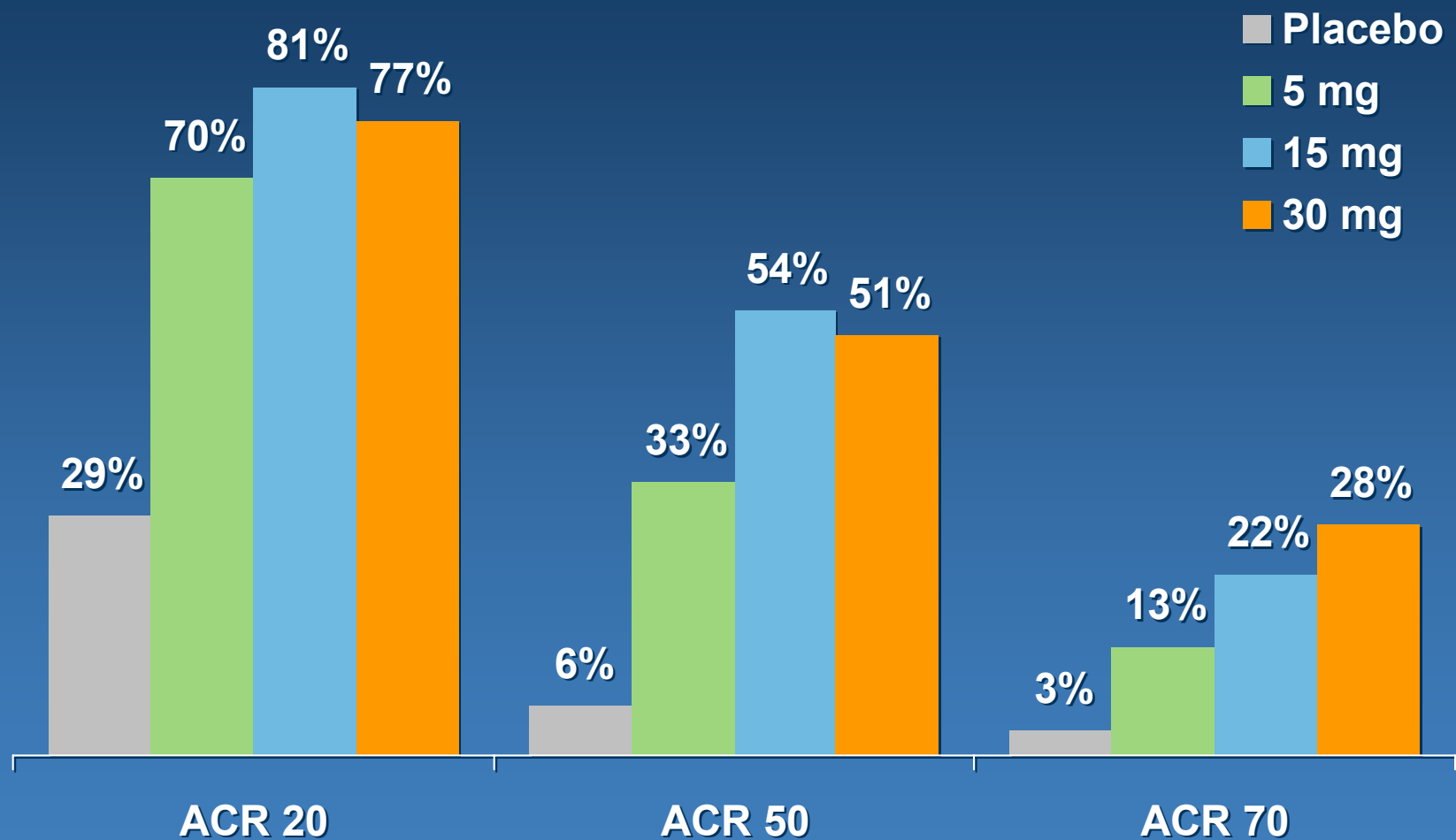
- Subjects with active RA who had failed either methotrexate  $\geq 15$  mg/wk or a TNF-inhibitor, but currently were on no DMARDs or biologics
- At least 9 tender and 6 swollen joints PLUS 2 of:
  - $\geq 45$  minutes AM stiffness;  $\geq 28$  mm/hr ESR;  $\geq 10$  mg/L CRP
- Background NSAIDs, analgesics, low-dose glucocorticoids allowed
- Equal randomization
- Study approved by local IRBs/ECs and all subjects provided written informed consent

# The ACR 20/50/70

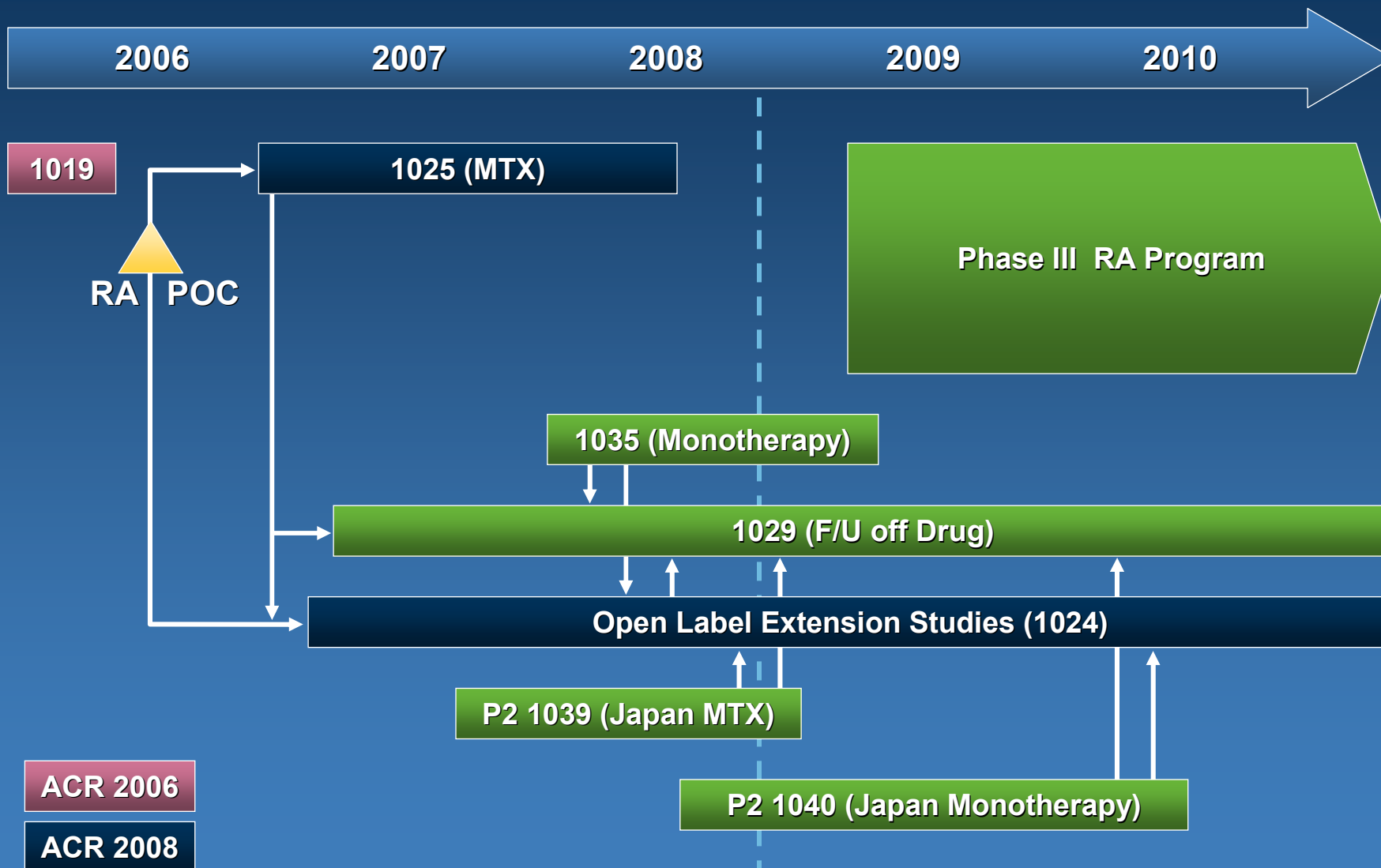
## ACR-20/50/70 Criteria Achieved When All of the Following Are True:

- 20/50/70% improvement from baseline in the tender joint count
- 20/50/70% improvement from baseline in the swollen joint count
- 20/50/70% improvement from baseline in *at least 3* of the 5 variables:
  - 1 Patient Global Assessment
  - 2 Physician Global Assessment
  - 3 Patient Pain Visual Analog Score (VAS)
  - 4 HAQ disability index
  - 5 C-Reactive Protein / Erythrocyte Sedimentation Rate (ESR)

# Study 1019: Week 6 ACR Response Rates



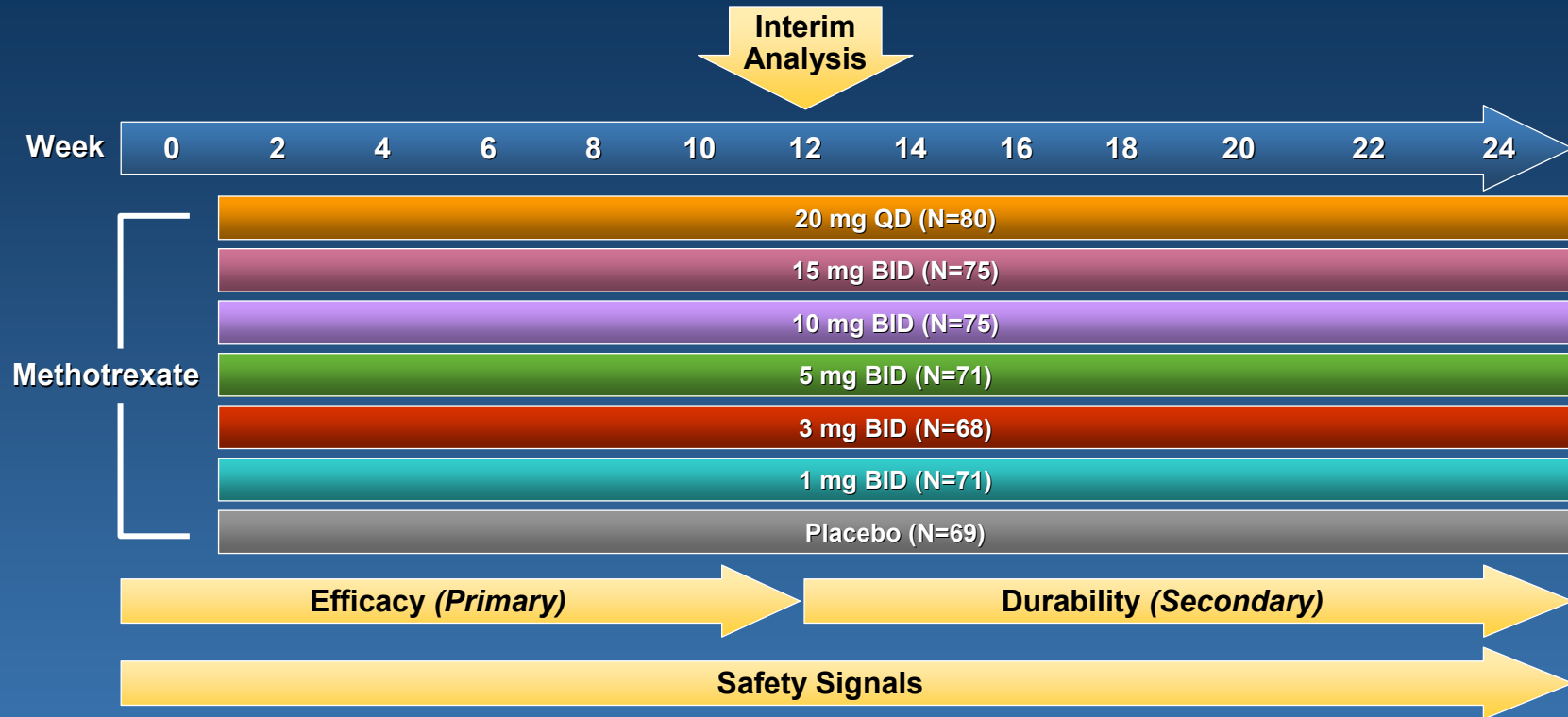
# CP-690,550 RA Program



# CP-690,550 Update

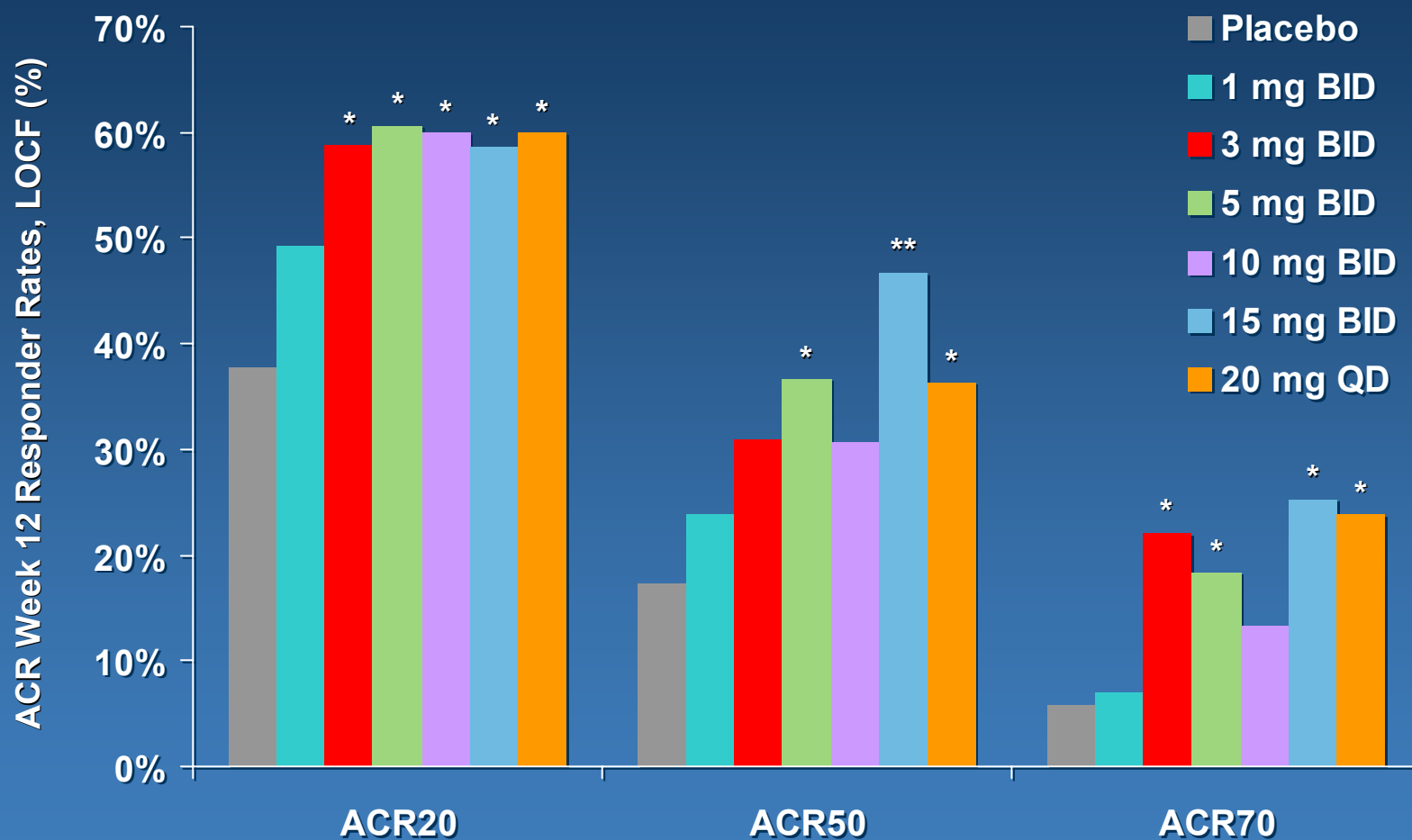
- Significant Unmet Need
- Mechanism of Action
- Review of Program and Previous RA Data
- **New Presentations at ACR**
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- Summary

# A3921025 Study Design



- Subjects with RA and inadequate response to stable dose (at least 6 weeks) MTX 7.5–25 mg/wk; if dosed <15 mg/wk, must have documented intolerance to or toxicity from higher doses
- At least 6 tender and 6 swollen joints and either CRP >7 mg/L OR ESR > ULN locally
- Background NSAIDs, analgesics, low-dose glucocorticoids allowed; DMARDs other than MTX washed out
- Equal randomization
- Subjects assigned to placebo, 1 mg BID, 3 mg BID or 20 mg QD who did not achieve at least 20% reduction in TJC and SJC at week 12 automatically advanced to 5 mg BID
- This study was approved by local IRBs/ECs and all subjects provided written informed consent

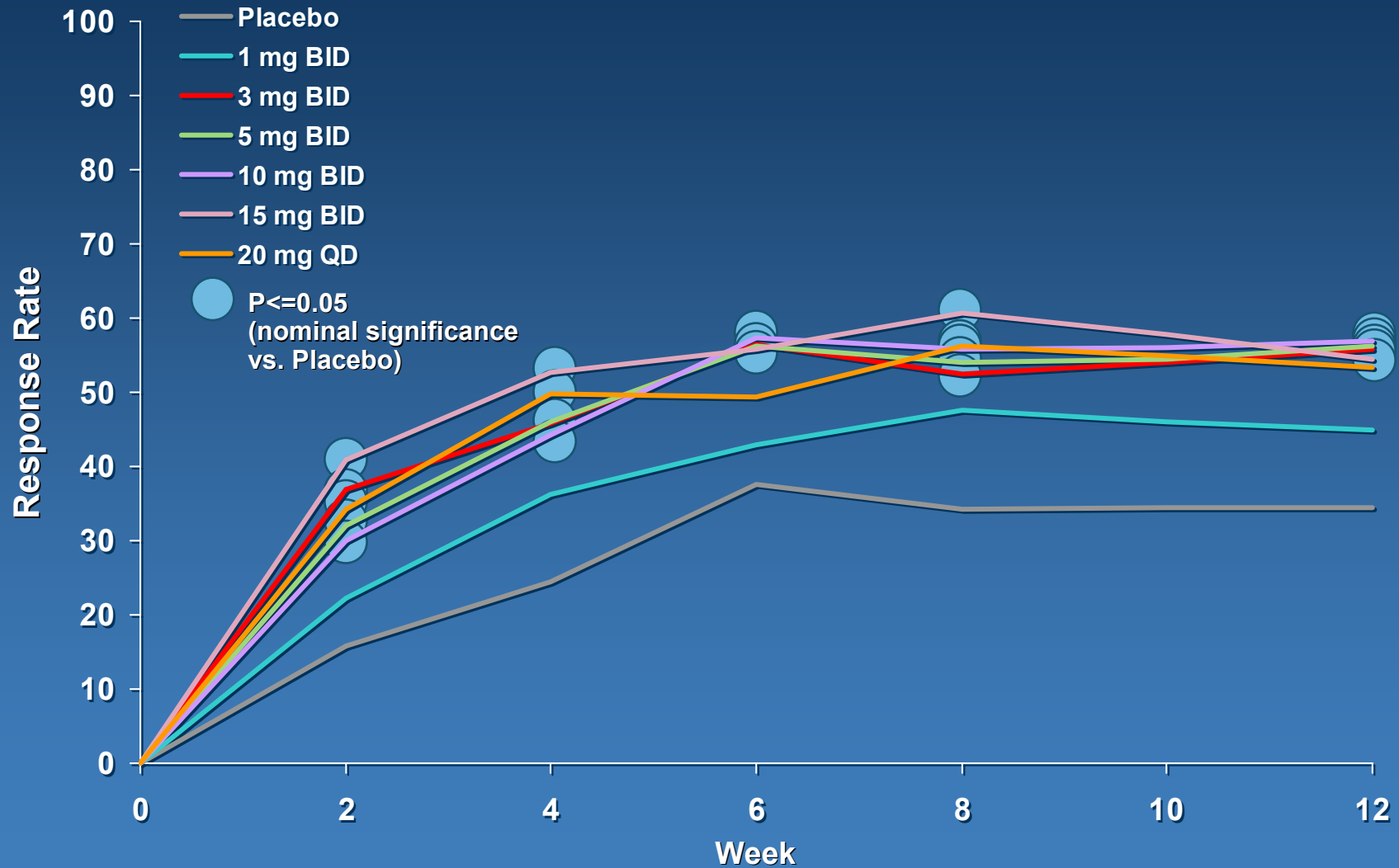
# Study 1025: Week 12 ACR Response Rates



\*  $p \leq 0.05$   
\*\*  $p \leq 0.0001$



# Study 1025: ACR 20 Response Rates Over Time



## Study 1025: Week 12 Efficacy Summary

- All doses except 1 mg bid showed a significantly better response than placebo, confirming efficacy from earlier 1019 study
- Efficacy generally improved with higher doses with maximal effects generally observed at 15 mg bid
- Onset of efficacy was as early as 2 weeks, peaked at 8 weeks and was maintained at 12 weeks

# Study 1025: Serious Infections

<b>Event</b>	<b>CP-690,550 Dose</b>	<b>MTX Weekly Dose</b>	<b>Age</b>
Pneumonia	3 mg BID	15 mg	40
Urinary tract infection	3 mg BID	15 mg	52
Pneumonia	5 mg BID	15 mg	56
Respiratory tract infection	10 mg BID	20 mg	68
Pneumonia	20 mg QD	17.5 mg	53

Serious infection was defined as one requiring hospitalization or parenteral antibiotic therapy; any subject with a serious infection was withdrawn from the study. All serious infections were observed in female study participants.



# Study 1025: Mean Changes from Baseline in HGB and ANC at Week 12

<b>Dose</b>	<b>HGB Change g/dl</b>	<b>Dose</b>	<b>ANC Change k/<math>\mu</math>l</b>
1 mg BID	0.02	1 mg BID	-0.80
3 mg BID	0.11*	3 mg BID	-0.50
5 mg BID	0.14*	5 mg BID	-0.82
10 mg BID	-0.42	10 mg BID	-0.83
15 mg BID	-0.40	15 mg BID	-1.18*
20 mg QD	-0.12	20 mg QD	-0.32
placebo	-0.18	placebo	-0.35

\* P < 0.05 compared to placebo



# Study 1025: Severe Anemia and Neutropenia

- 3 subjects had ANC's less than 1000 k/ $\mu$ l
  - 15 mg bid
  - 15 mg bid
  - 1 mg bid
- No potentially life threatening cases of neutropenia (< 500 k/ $\mu$ l)

## Incidence Through Week 12 of Subjects with Anemia That Is Severe or Life Threatening

Dose	N	n	Anemia Rates	
			Observed	Above Placebo
placebo	67	2	3.0%	
1 mg BID	69	3	4.4%	1.4%
3 mg BID	67	2	3.0%	0.0%
5 mg BID	70	1	1.4%	-1.6%
10 mg BID	73	5	6.9%	3.9%
15 mg BID	73	6	8.2%	5.2%
20 mg QD	79	2	2.5%	-0.5%

Severe or Life-threatening Anemia (combined), defined by OMERACT as a decrease of at least 2.1 G/dL or a hemoglobin < 8 G/dL



# Study 1025: Incidence of Transaminase Elevations (Subjects with Normal BL)

	AST > 3 X ULN	ALT > 3 X ULN
1 mg BID	0	0
3 mg BID	0	0
5 mg BID	0	0
10 mg BID	1 (1%)	1 (1%)
15 mg BID	2 (3%)	4 (5%)
20 mg QD	2 (3%)	1 (1%)
placebo	0	1 (2%)

No subject met “Hy’s rule”: ALT > 3 X ULN and Bilirubin > 2 X ULN



# Study 1025: Mean Changes from Baseline in HDL and LDL at Week 12

<b>Dose</b>	<b>HDL Change mg/dl</b>	<b>Dose</b>	<b>LDL Change mg/dl</b>
1 mg BID	2.22*	1 mg BID	6.31**
3 mg BID	3.63**	3 mg BID	8.14**
5 mg BID	6.11**	5 mg BID	12.97**
10 mg BID	2.71*	10 mg BID	16.17**
15 mg BID	4.74**	15 mg BID	15.23**
20 mg QD	5.78**	20 mg QD	9.61**
placebo	-1.32	placebo	-5.15

\* P < 0.05 compared to placebo

\*\* P < 0.005 compared to placebo



# Study 1025: Safety Summary (Week 12)

- Serious infections were few and not dose responsive
- Dose related changes in hemoglobin and neutrophils were seen. Incidences of OMERACT severe or life-threatening anemia and neutropenia were low. No subject was withdrawn for protocol specified hemoglobin or neutrophil levels
- Small increases in serum creatinine over baseline were seen in all dose groups, including placebo. No increases were progressive over time compared to placebo
- Dose dependent increases in LDL, HDL and total cholesterol were observed, but increases appeared to plateau by week 6
- Increased incidences of potentially significant ALT increases were observed in the 15 mg BID dose

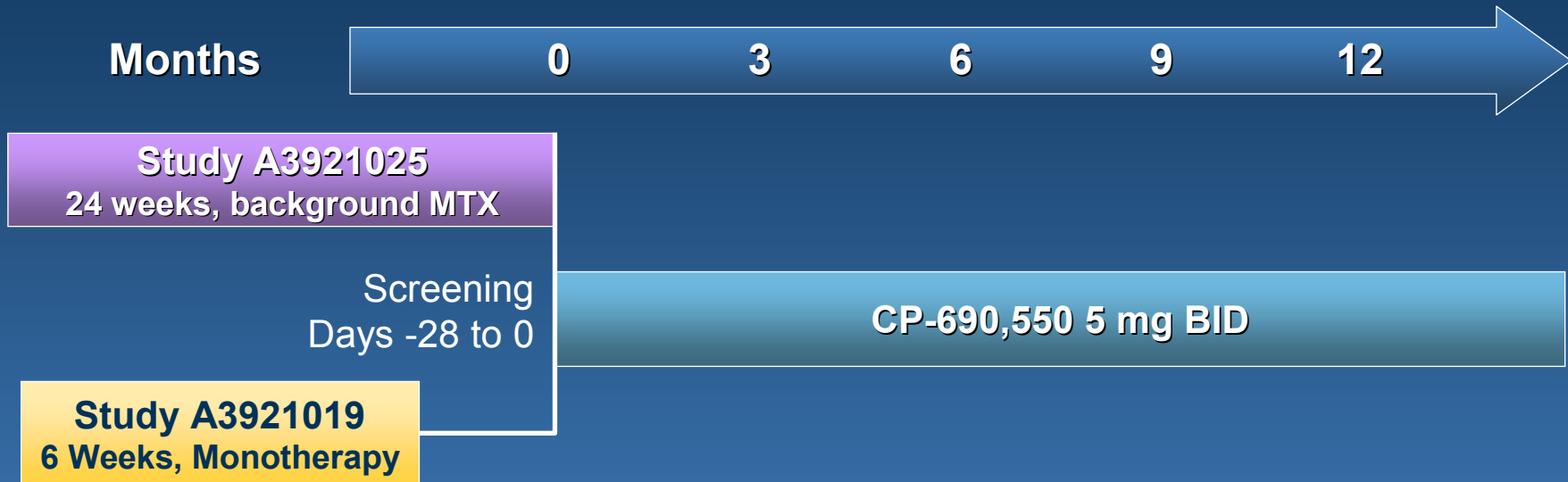
## **Study 1025: Overall Conclusions**

- **An efficacy and safety profile justifying progression to Phase III was observed**
- **The data presented, plus the 24 week data from this study, plus data anticipated from study 1035 will provide a robust database to inform Phase III dosing**

# CP-690,550 Update

- Significant Unmet Need
- Value Proposition and Mechanism
- Review of Program and Previous RA Data
- **New Presentations at ACR**
  - 12 week dose response data (study 1025)
  - **Open Label Extension (study 1024)**
  - MTX DDI Study (study 1013)
- Summary

# Study A3921024: Open-label, Long-term, Multicenter Study



- Patients could continue their stable background RA therapy, including approved DMARDs and glucocorticoids
- Specific rescue medications and adjustments of background therapy were allowed
- Study approved by local IRBs / ECs. All subjects gave written informed consent

## **Study 1024: Interim Analysis**

- **An interim analysis was conducted of all safety data for all 129 patients enrolled as of 22-Feb-2008**
- **Comparisons in laboratory data and DAS were made at 1 and 6 months**
  - **40 patients had completed 6 months in study as of 22-Feb-2008**

## Study 1024: Adverse Events\* in 129 Subjects

- **Total AEs = 160**
  - Mild = 93
  - Moderate = 64
  - Severe = 3 (myocardial infarction, RA, acne)
- **Infections = 32**
  - Mild = 13
  - Moderate = 19
  - Severe = 0
  - No serious AE's related to infection by data cut

\* At time of Feb 22, 2008 data cut



# Study 1024: Laboratory Values at 6 Months

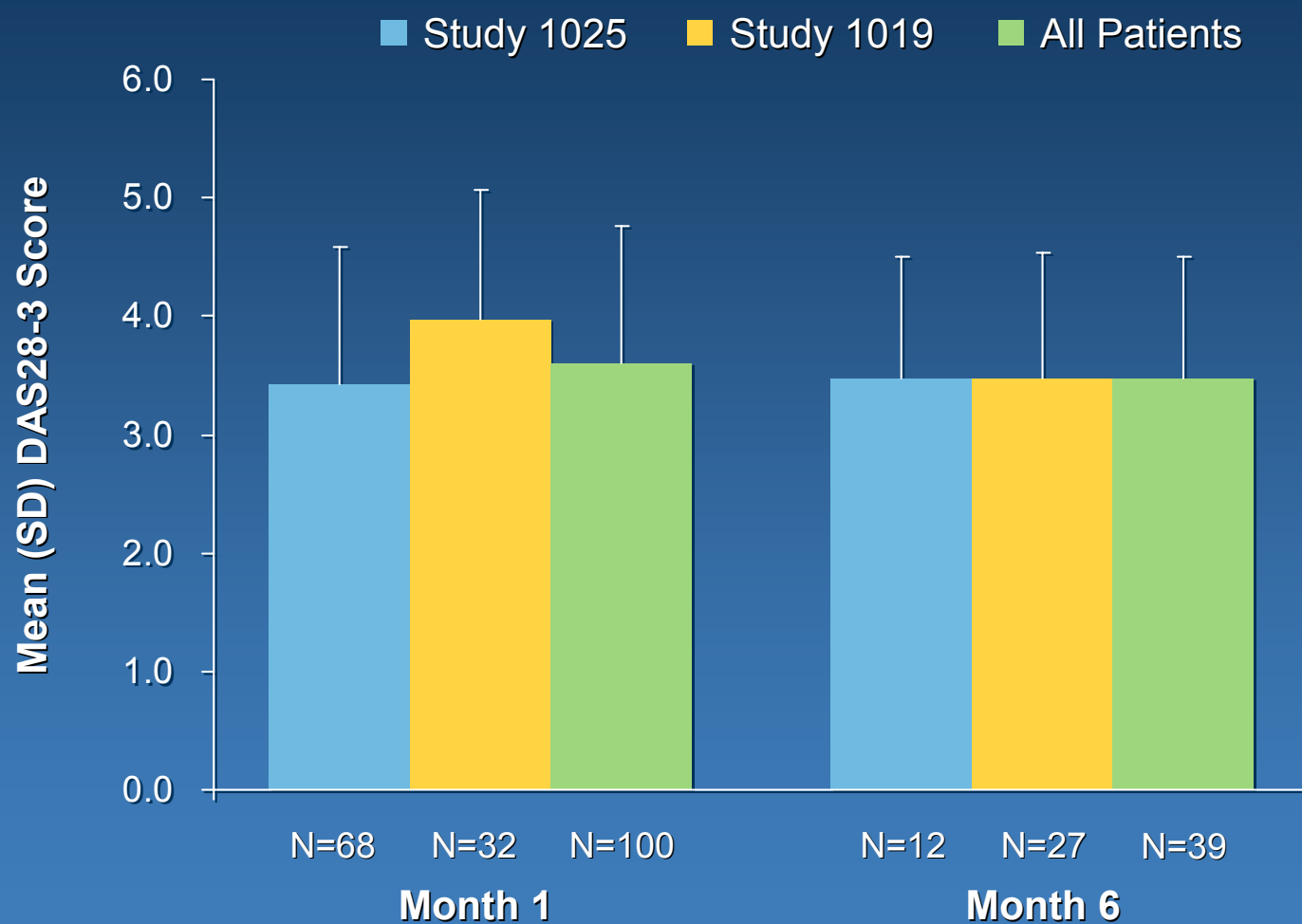
## CP-690,550 5 mg BID

	1025	1019	All
Serum creatinine, mg/dL	0.92 ± 0.23	0.86 ± 0.20	0.88 ± 0.21
Neutrophil count, 10 <sup>3</sup> /mm <sup>3</sup>	5.27 ± 1.56	5.01 ± 1.81	5.09 ± 1.73
Hemoglobin, g/dL	12.31 ± 0.91	13.70 ± 1.30	13.28 ± 1.35
LDL, mg/dL	117.02 ± 34.36	145.45 ± 34.90	136.92 ± 36.74
HDL, mg/dL	69.43 ± 27.30	62.44 ± 15.81	64.54 ± 19.84

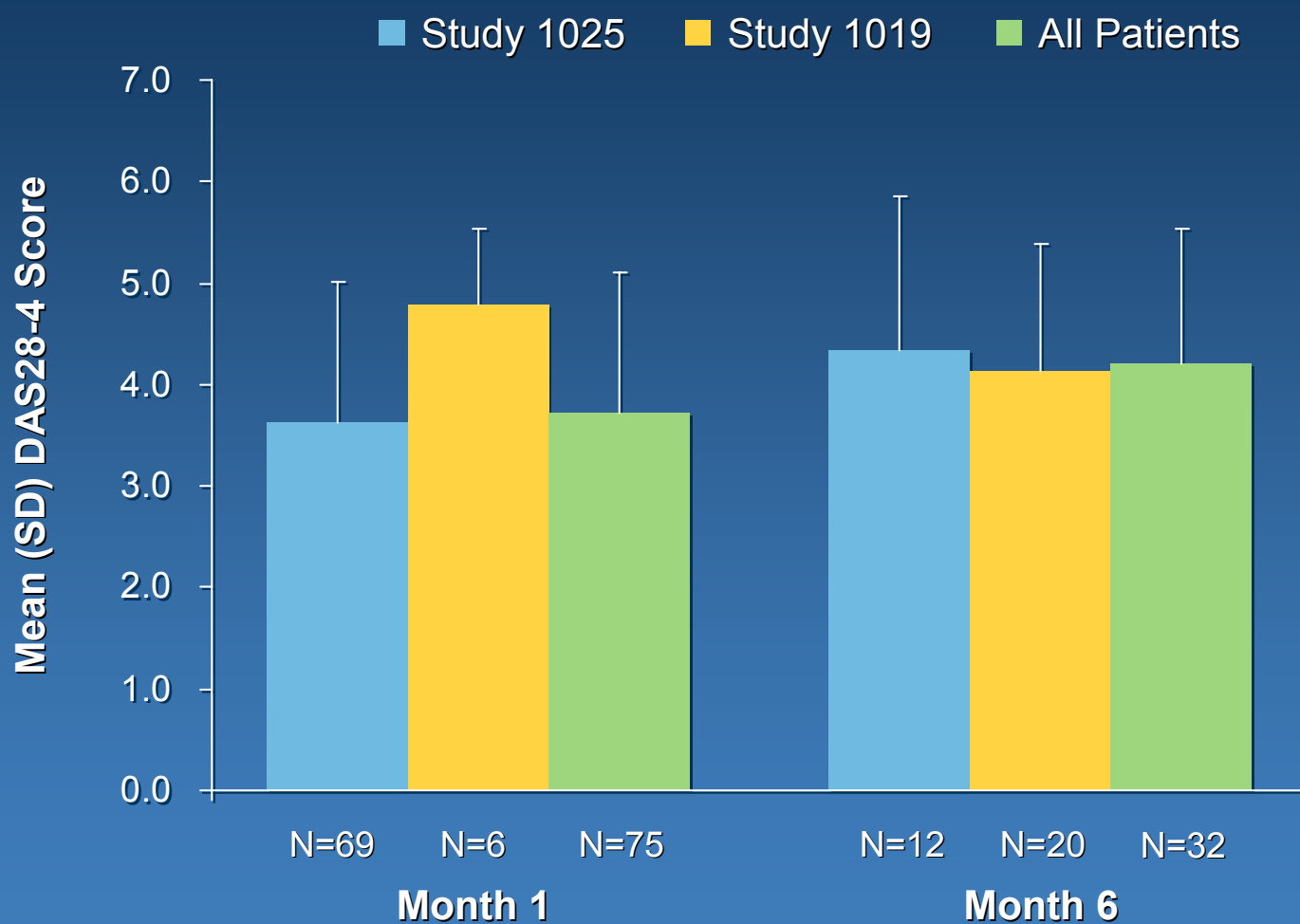
Data presented as mean ± SD



# Study 1024: DAS28-3 (CRP)



# Study 1024: DAS28-4 (ESR)



## Study 1024: Conclusions

- CP-690,550 5 mg BID was well tolerated and efficacious in patients with moderate to severe active RA over a median of 109.0 days
- DAS 28 was similar in all patients at 6 months, regardless of prior study experience
- Mean laboratory values remained within normal limits at 6 months; no patient required discontinuation due to individual changes in laboratory values

# CP-690,550 Update

- Significant Unmet Need
- Value Proposition and Mechanism
- Review of Program and Previous RA Data
- **New Presentations at ACR**
  - 12 week dose response data (study 1025)
  - Open Label Extension (study 1024)
  - **MTX DDI Study (study 1013)**
- Summary

# Study 1013: MTX DDI Study Summary

- **Study Objectives:**

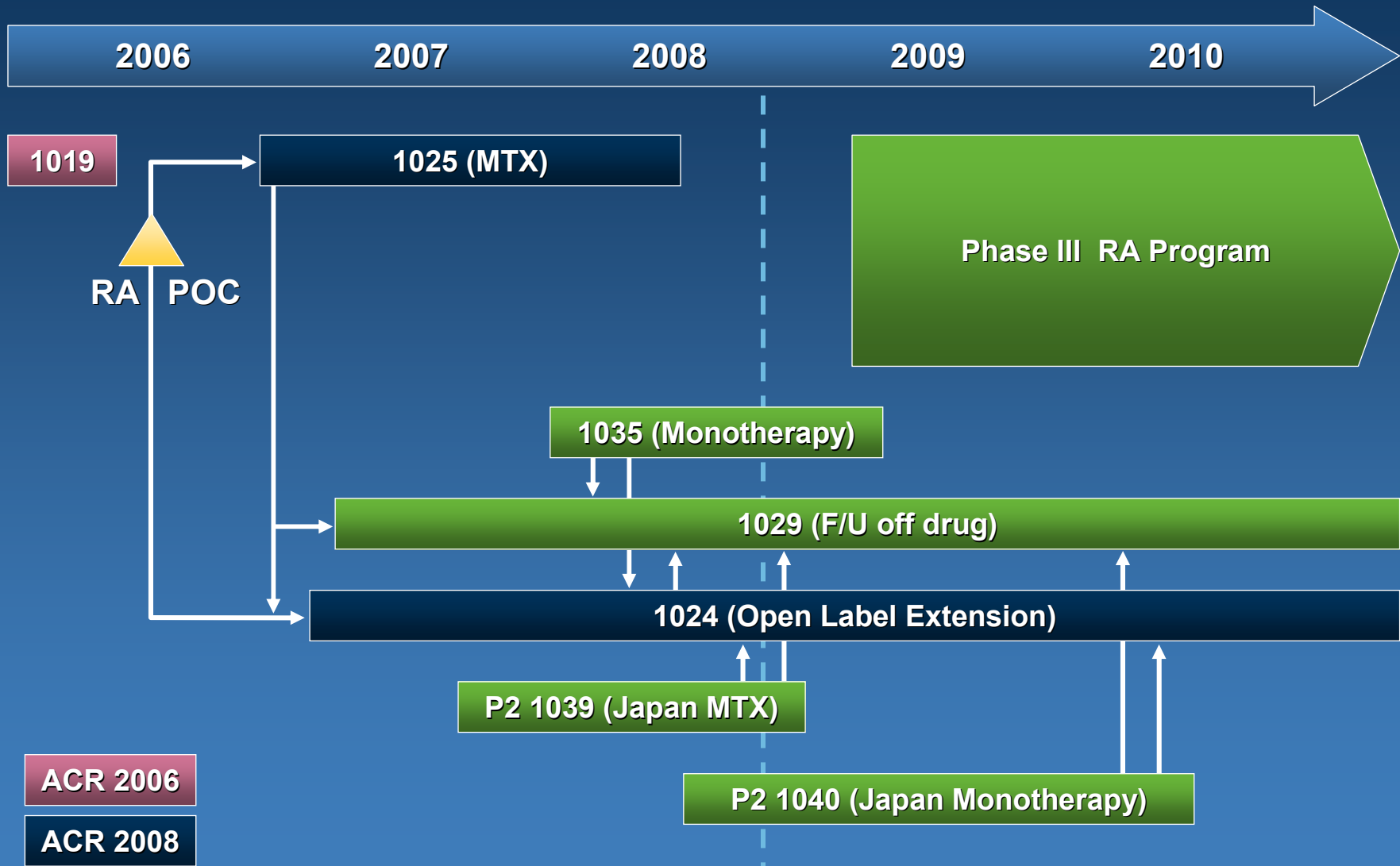
- To estimate the effects of MTX on the pharmacokinetics (PK) of CP-690,550 when administered to subjects with RA
- To estimate the effects of multiple doses of CP-690,550 (30 mg Q 12 h) on the PK of MTX
- To evaluate the short-term safety and tolerability of co-administration of CP-690,550 (30 mg Q 12 h) and MTX

- **Conclusions:**

- Co-administration of CP-690,550 and MTX in RA subjects appeared to be safe and well tolerated
- MTX had no clinically relevant effect on the CP-690,550 PK
- CP-690,550 had no clinically relevant effect on MTX AUC values and the observed 10% increase in MTX C<sub>max</sub> value when co-administered with CP-690,550 is not expected to be clinically important
- Therefore, based on the PK results from this study, no dosage adjustment is needed when co-administering CP-690,550 and MTX



# CP-690,550 RA Program



## Conclusion

- **Current products for RA have significant limitations**
- **CP-690,550 may offer benefits of both a small molecule and a biologic**
- **Data to date for CP-690,550 has demonstrated a promising profile**
- **Robust clinical program underway / Plans for Phase III trial progressing**



**Q&A**