# CP-690,550 Update

**EULAR**

**June 12, 2009**

# Forward-Looking Statements and Non-GAAP Financial Information

- Our discussions during this presentation 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 2008 Annual Report on Form 10-K and in our reports on Form 10-Q and Form 8-K.
- These reports are available on our website at **www.pfizer.com** in the "Investors—SEC Filings" section.

# CP-690,550 Update

**Bernhardt Zeiher, M.D.**
**Inflammation Disease Area Lead**

**Copenhagen, June 2009**

# CP-690,550 Update

- Compound overview and mechanism of action
- Overview of Phase 2 RA Program
- New presentations at EULAR
  - 12 week interim analysis of 6-month monotherapy study (Study 1035)
  - 12-week Japanese study on background MTX (Study 1039)
  - Update on Open Label Extension study (Study 1024)
- Summary and overview of Phase 3 Program

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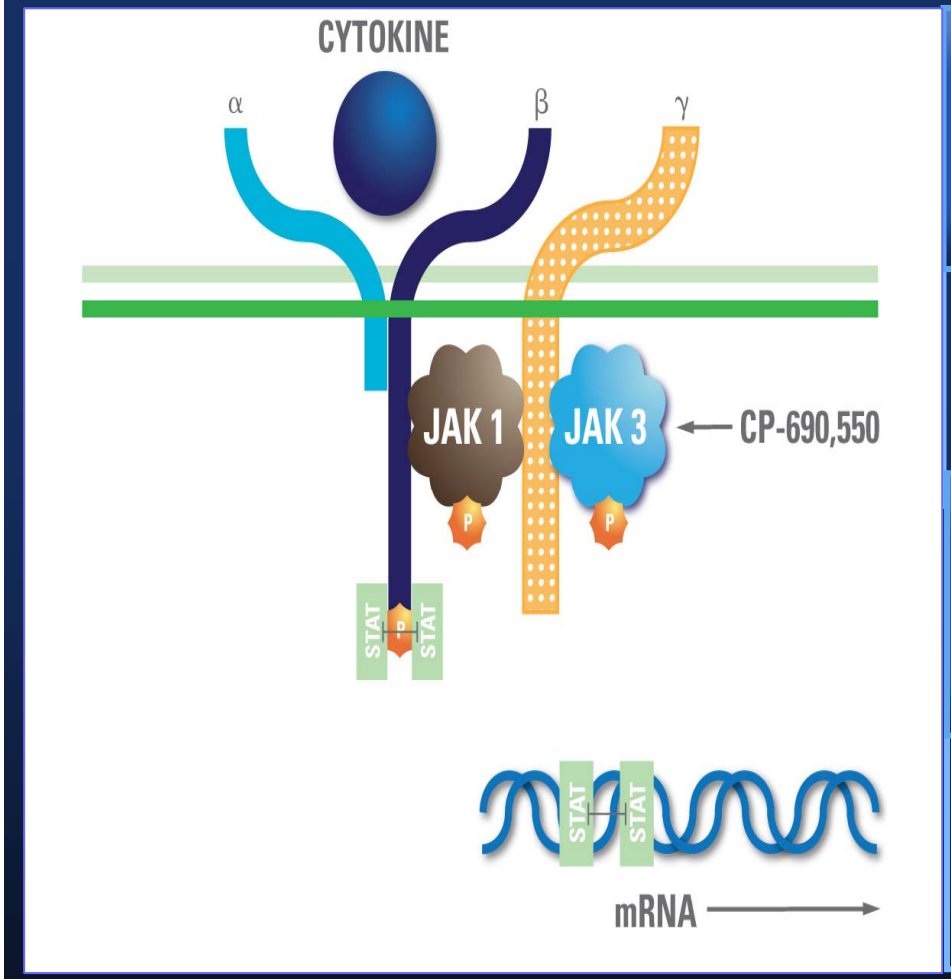
# CP-690,550 – A Potentially Exciting New Development in the Treatment of RA

- 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 with RA as well as a number of other autoimmune diseases

# Pharmacology of CP-690,550

- CP-690,550 is an orally available, highly selective inhibitor of the Janus kinase (JAK) family of enzymes
- Pharmacokinetics are dose proportional ("well behaved"), t½: 2 to 5 hours
- Primarily eliminated by urinary excretion; 30% unchanged
- Substrate for CYP3A4/5 (with limited metabolism through 2C19)
- Preliminary efficacy has been demonstrated in rheumatoid arthritis, psoriasis and renal allograft transplantation

# CP 690,550 is a Selective Inhibitor of Janus Kinases



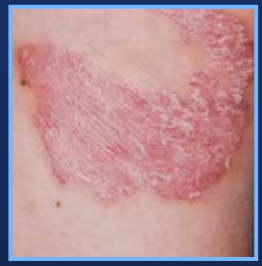
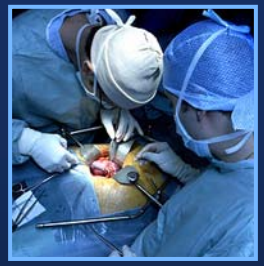
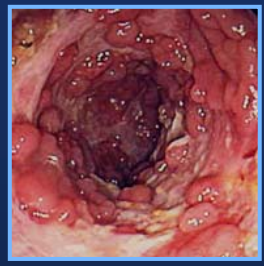
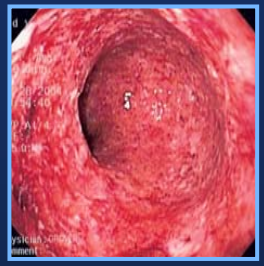
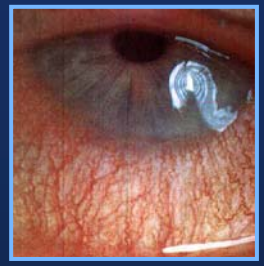

**Cytokines Signaling Through JAK1/3**

**IL-2, IL-4, IL-7, IL-9, IL-15, IL-21**

**Cytokines Signaling Through Other JAK1 Combinations**

**IL-6, IFNγ, IFNα/β, IL-22, IL-34**

# CP-690,550 is Being Evaluated in a Number of Inflammatory and Immunologic Diseases

| Indications | Rheumatoid Arthritis | Psoriasis | Transplant | Crohn's Disease | Ulcerative Colitis | Dry Eye |
|---|---|---|---|---|---|---|
| Disease Burden |  |  |  |  |  |  |
| Phase | III | IIb | IIb | IIa | IIa | IIa |

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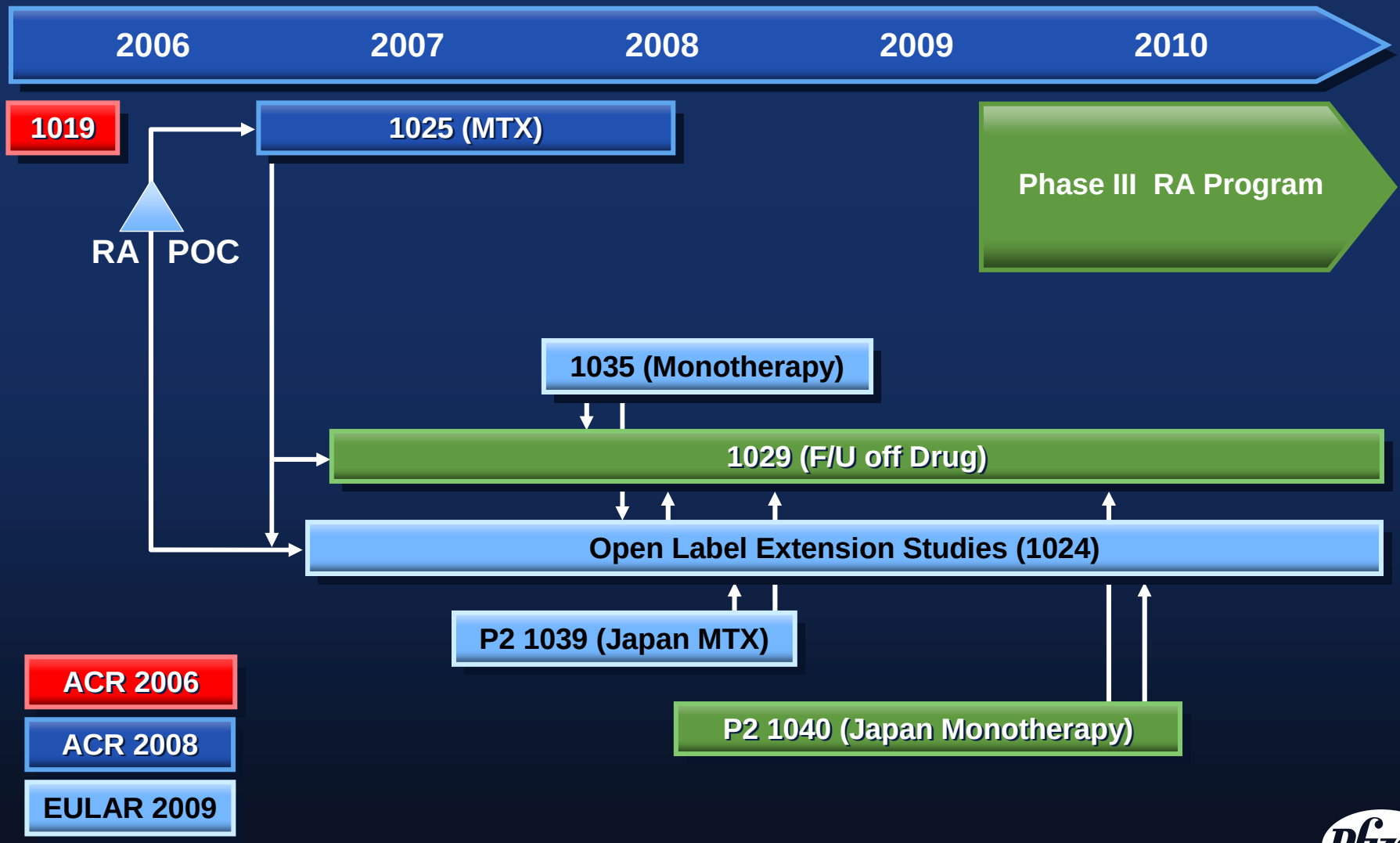
# CP-690,550 Phase 2 RA Program

- Extensive Phase 2 Program
  - 6-week monotherapy POC study (Study 1019)
  - 24-week Phase 2b study on background MTX (Study 1025)
  - 24-week Phase 2b Monotherapy Study (Study 1035)
  - 12-week Phase 2b Japanese study on background MTX (Study 1039)
  - Patients enrolled in Studies 1019, 1025 and 1035 have the option of enrolling in long-term open-label extension study (Study 1024)
- Explored dose range of 1 to 30 mg BID
- >1,000 patients enrolled across the Phase 2 Program

**Largest Mid-Stage Program Ever Conducted in RA**

# CP-690,550 RA Program



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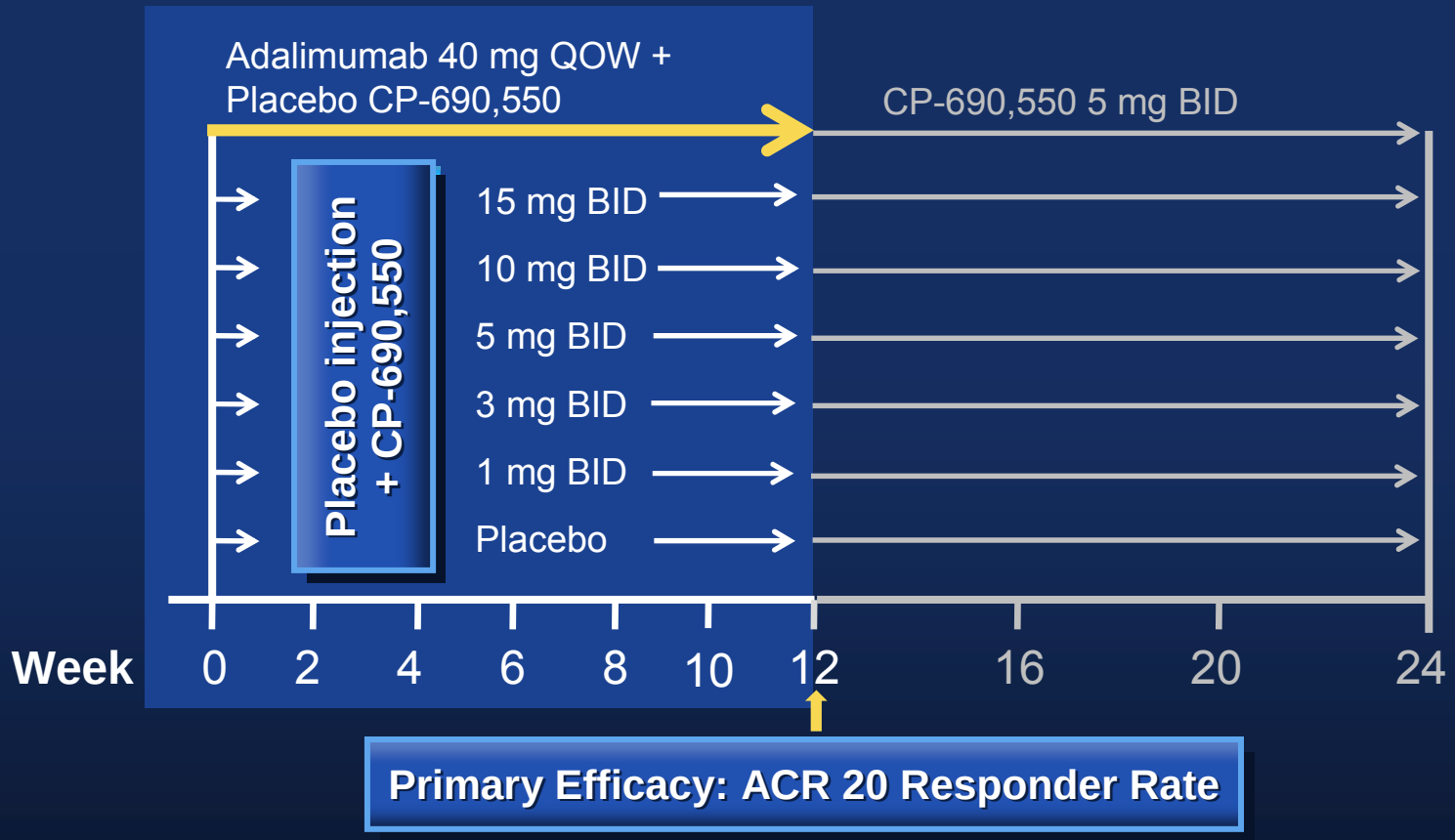
# Definition of ACR Response

**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 1035: 6-Month Monotherapy, in Inadequate Responders to DMARDs




- Patients in the 1 mg BID, 3 mg BID and placebo groups who failed to achieve an improvement from baseline of ≥ 20% in both tender and swollen joint counts at Week 12 were automatically reassigned to 5 mg BID
- This study was approved by local IRBs / ECs and all subjects provided written informed consent
- All data presented are from the week 12 interim analysis and based upon complete data to week 12 only

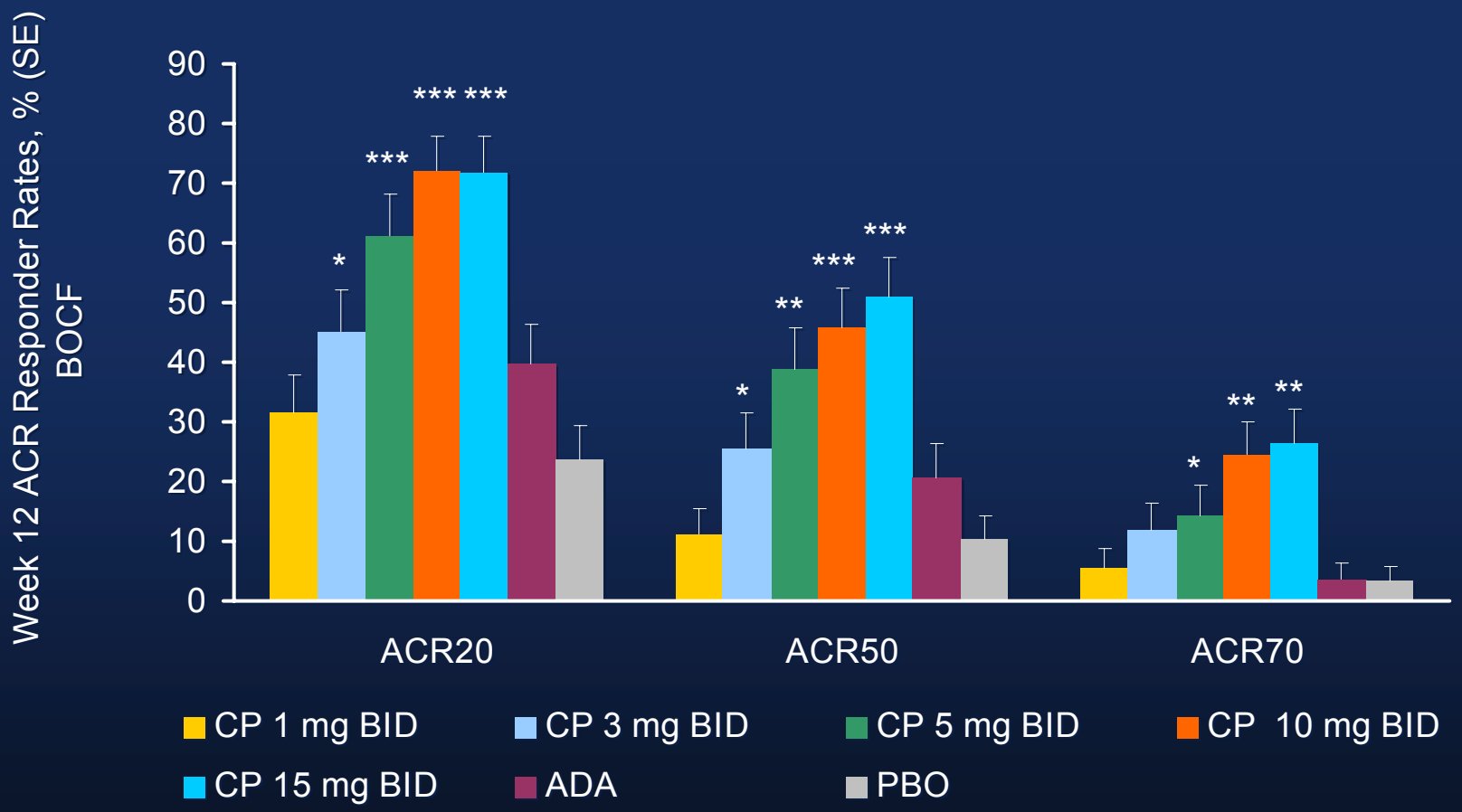
# Study 1035: Patient Disposition (Week 0-12)

| Treatment Group | | D / C | D / C for Adverse Events | D / C For Adverse Events That May Be Treatment-related | D / C for Lack of Efficacy |
|---|---|---|---|---|---|
| | N | N(%) | N(%) | N(%) | N(%) |
| CP-690,550 | | | | | |
| **1 mg BID** | **54** | **10 (18.5)** | **2 (3.7)** | **1 (1.9)** | **3 (5.6)** |
| 3 mg BID | 51 | 4 (7.8) | 2 (3.9) | 0 | 1 (2.0) |
| 5 mg BID | 49 | 3 (6.1) | 0 | 0 | 0 |
| 10 mg BID | 61 | 3 (4.9) | 0 | 0 | 1 (1.6) |
| 15 mg BID | 57 | 3 (5.3) | 2 (3.5) | 2 (3.5) | 0 |
| **Adalimumab** | **53** | **8 (15.1)** | **2 (3.8)** | **2 (3.8)** | **3 (5.7)** |
| **Placebo** | **59** | **13 (22.0)** | **1 (1.7)** | **0** | **3 (5.1)** |



D / C, discontinuation

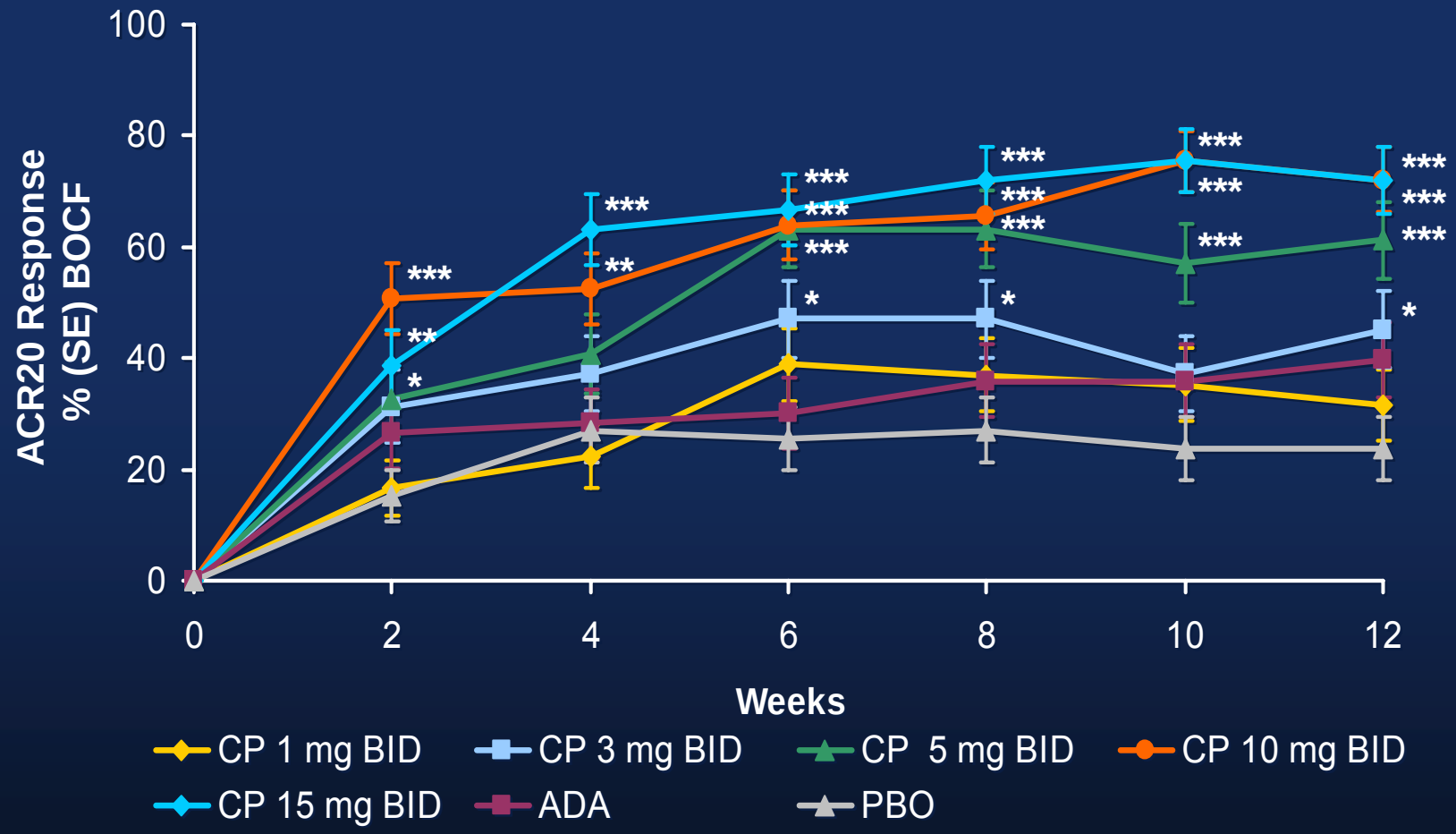
# Study 1035: Week 12 ACR Response Rate (nonresponder imputation)




Difference from placebo *p<0.05; **p<0.001; ***p<0.0001

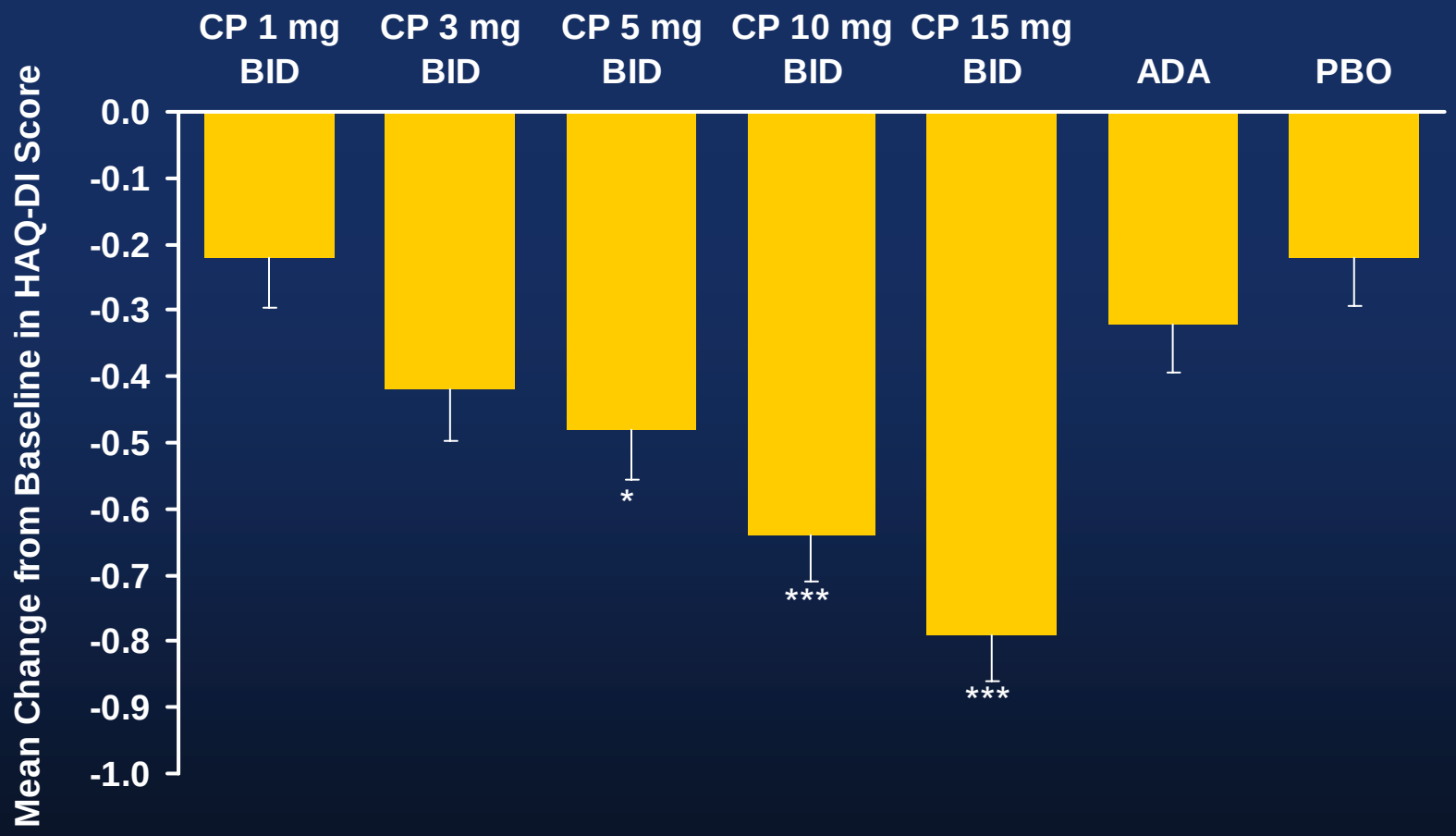
ADA, adalimumab; CP, CP-690,550; BOCF, baseline observation carried forward; PBO, placebo

# Study 1035:
# Time Course of ACR20 Response




Difference from placebo *p<0.05; **p<0.01; ***p<0.001
BOCF, baseline observation carried forward

# Study 1035: Change in HAQ-DI Score at Week 12




Difference from placebo *p<0.05; **p<0.001; ***p<0.0001
ADA, adalimumab; CP, CP-690,550; PBO, placebo

# Study 1035: Most Common Treatment-Emergent AEs

## *(≥5% in Any Treatment Group, Baseline to Week 12)*

| MedDRA Preferred Term, n (%) | CP-690,550 (mg BID) | | | | | ADA | PBO |
|---|---|---|---|---|---|---|---|
| | 1 | 3 | 5 | 10 | 15 | | |
| **n** | **54** | **51** | **49** | **61** | **57** | **53** | **59** |
| Urinary tract infection | 2 (3.7) | 1 (2.0) | 5 (10.2) | 2 (3.3) | 4 (7.0) | 2 (3.8) | 3 (5.1) |
| Headache | 0 | 2 (3.9) | 2 (4.1) | 5 (8.2) | 2 (3.5) | 2 (3.8) | 1 (1.7) |
| Bronchitis | 1 (1.9) | 2 (3.9) | 2 (4.1) | 1 (1.6) | 4 (7.0) | 3 (5.7) | 1 (1.7) |
| Diarrhea | 2 (3.7) | 2 (3.9) | 2 (4.1) | 4 (6.6) | 1 (1.8) | 1 (1.9) | 1 (1.7) |
| Pruritus | 0 | 0 | 0 | 1 (1.6) | 0 | 3 (5.7) | 0 |
| Chest discomfort | 0 | 0 | 0 | 0 | 3 (5.3) | 0 | 0 |
| Dizziness | 2 (3.7) | 0 | 0 | 2 (3.3) | 3 (5.3) | 2 (3.8) | 1 (1.7) |
| Rash | 1 (1.9) | 0 | 1 (2.0) | 0 | 3 (5.3) | 2 (3.8) | 1 (1.7) |



Patients counted once per treatment in each row

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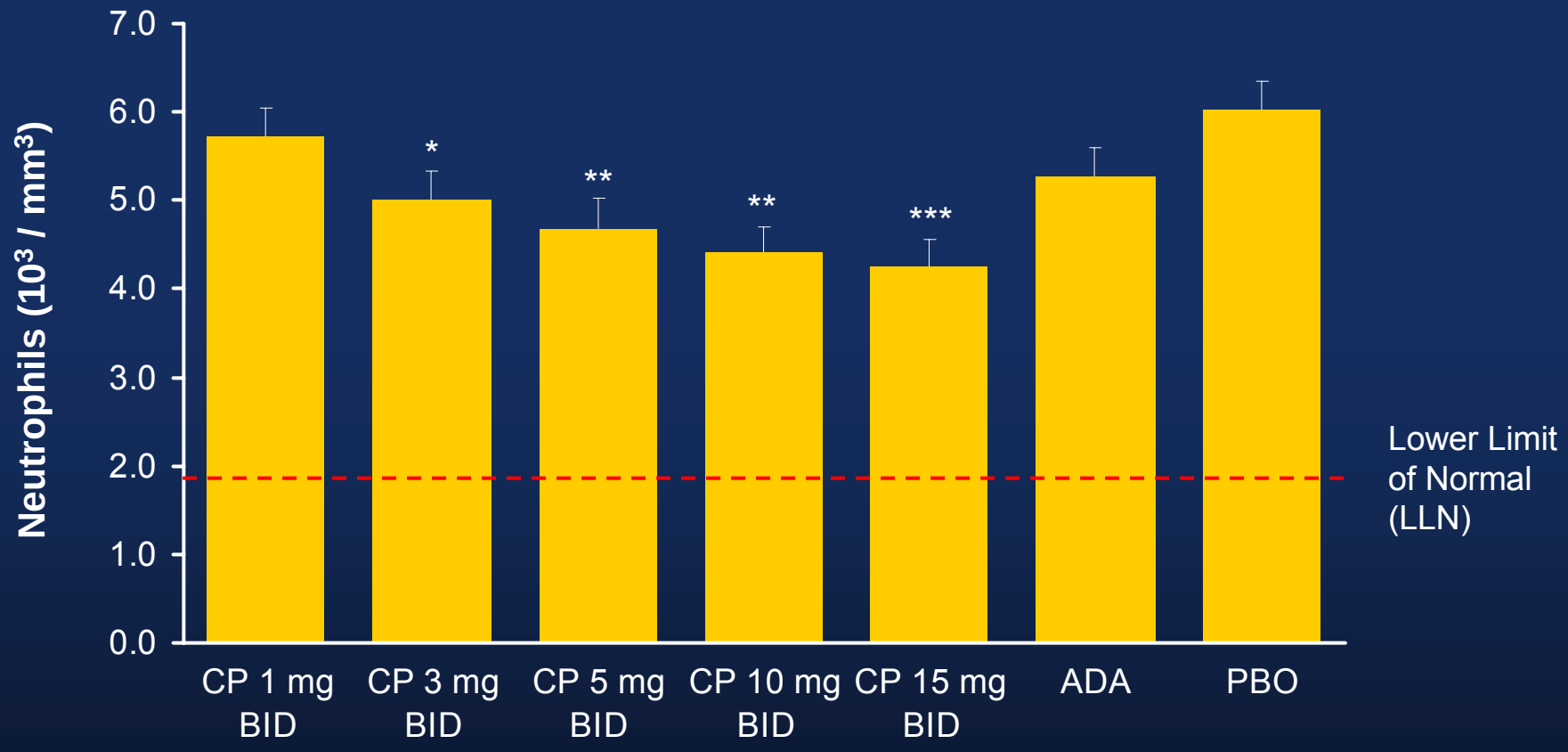
# Study 1035:
# Serious AEs (Baseline-Week 12)

| Dose | Serious Adverse Event |
|---|---|
| **1 mg BID** | None |
| **3 mg BID** | Anemia/Gastric Ulcer |
| **5 mg BID** | None |
| **10 mg BID** | None |
| **15 mg BID** | Gastritis, Pneumonia Pneumococcal |
| **Adalimumab** | Renal cell carcinoma, Total knee replacement |
| **Placebo** | Panic Attack |



Based upon week 12 interim analysis

# Study 1035: Absolute Neutrophil Count at Week 12

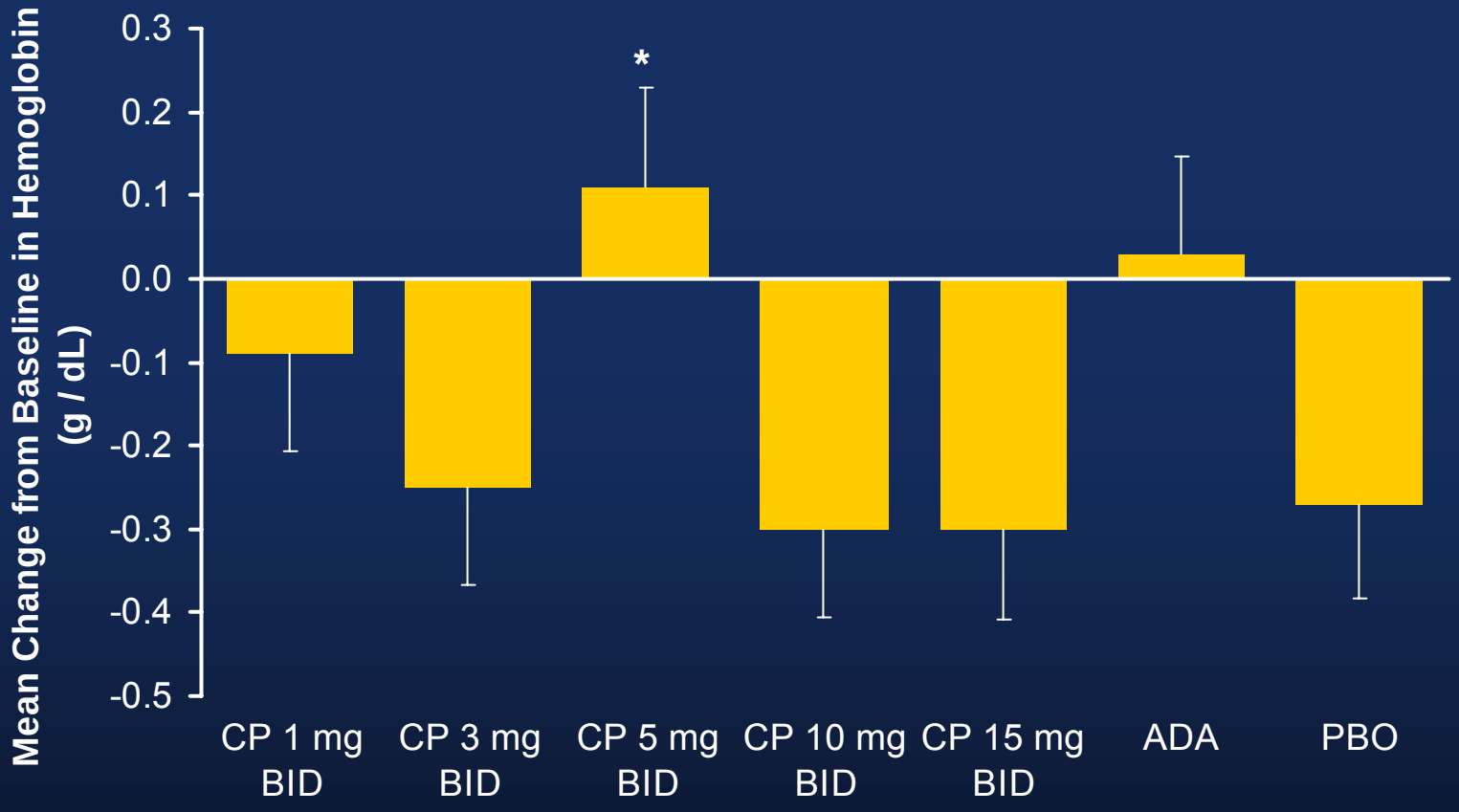



**No Cases of Severe Neutropenia or Discontinuations Due to Neutropenia**

Difference from placebo *p<0.05; **p<0.001; ***p<0.0001

ADA, adalimumab; CP, CP-690,550; LOCF, last observation carried forward; PBO, placebo

# Study 1035: Change in Hemoglobin at Week 12



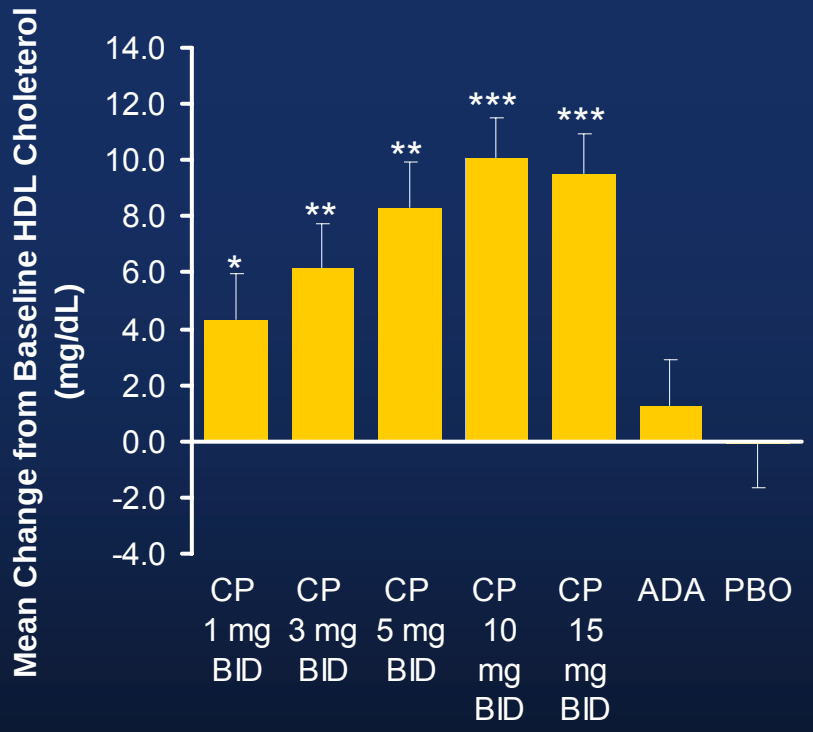

**No Significant Decrease in Hemoglobin**

Difference from placebo *p<0.05; **p<0.001; ***p<0.0001

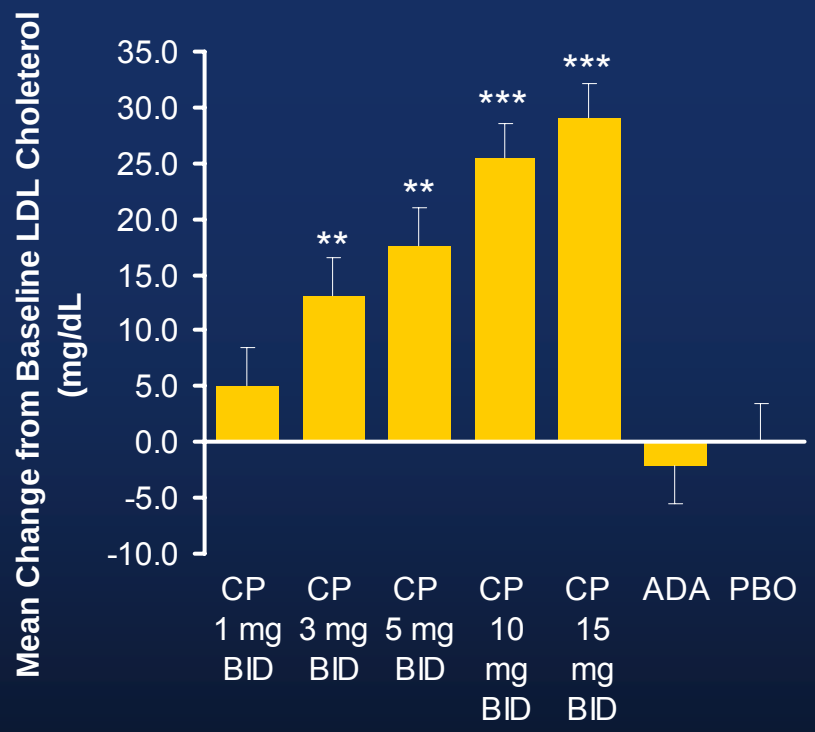
ADA, adalimumab; CP, CP-690,550; LOCF, last observation carried forward; PBO, placebo

# Study 1035: Change in HDL and LDL Cholesterol at Week 12

## HDL




## LDL




**Dose Dependent Increases in HDL and LDL**

Difference from placebo *p<0.05; **p<0.001; ***p<0.0001

ADA, adalimumab; CP, CP-690,550; LOCF, last observation carried forward; PBO, placebo

# Study 1035: Summary of Interim Analysis

- CP-690,550 dosed 3 – 15 mg BID was superior to placebo in ACR20 and ACR50 response rates at week 12
  - Responses were rapid with separation from placebo in ACR20 response at the earliest time point of 2 weeks
- CP-690,550 dosed 5 – 15 mg BID was superior to placebo in ACR70 response rates at week 12 and changes from baseline in the HAQ-DI
- No significant decreases in mean hemoglobin
- Significant, dose-dependent decreases in mean neutrophil counts, but no severe neutropenia or discontinuations due to neutropenia
- Increases in mean LDL, HDL, total cholesterol consistent with what has been observed in previous studies of CP-690,550 in RA
- No dose response for significant infections
- No opportunistic infections seen.



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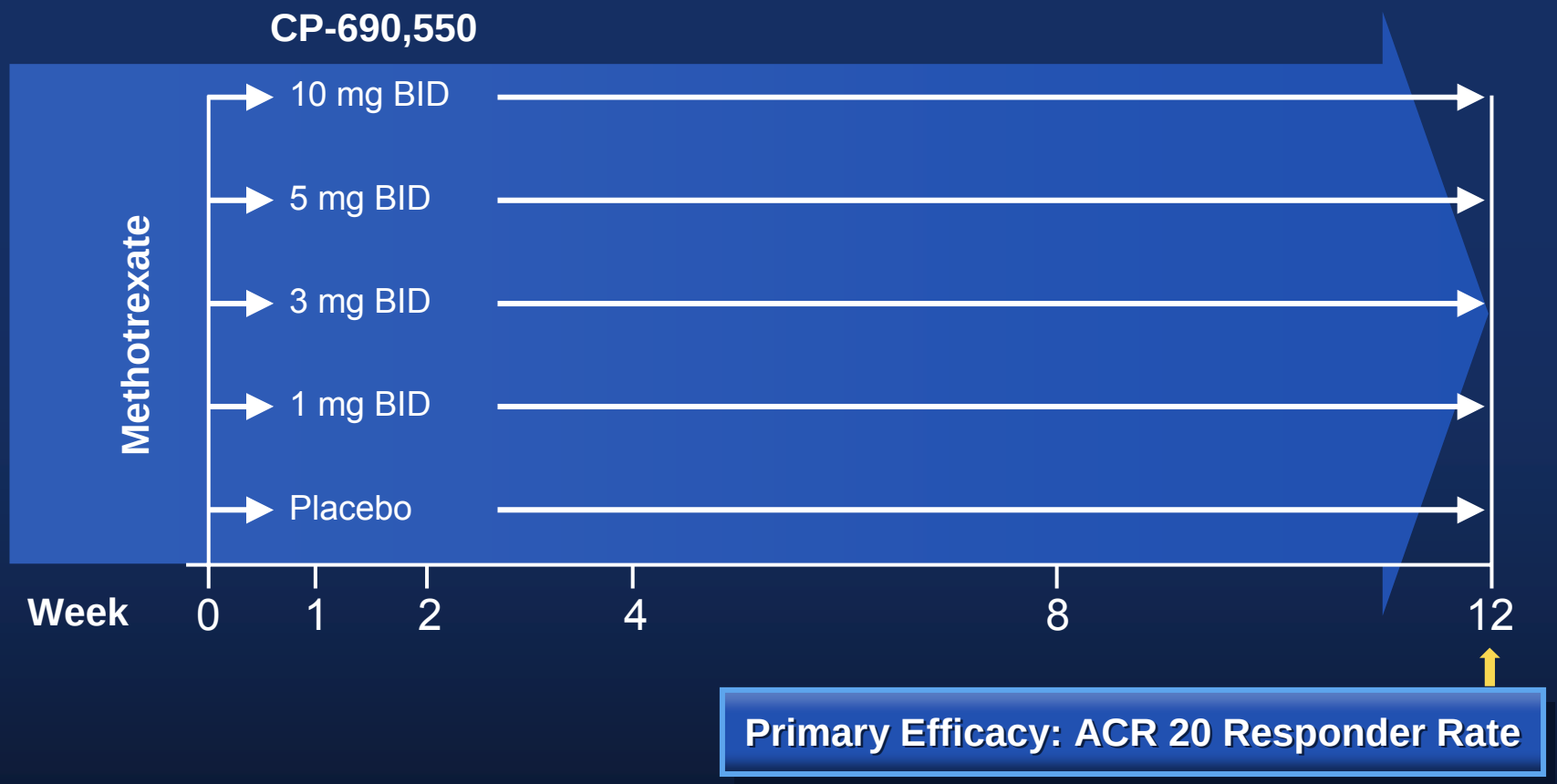
# Study 1039: A 12-Week Phase 2 Japanese Study on Background Methotrexate




- Patients must have received MTX for at least 4 months consecutively, and must have received doses of at least 6 mg / week from at least 6 weeks prior to baseline
- At least 6 tender and 6 swollen joints PLUS ≥7 mg/L CRP or abnormal ESR
- Background NSAIDs, analgesics, low-dose glucocorticoids allowed

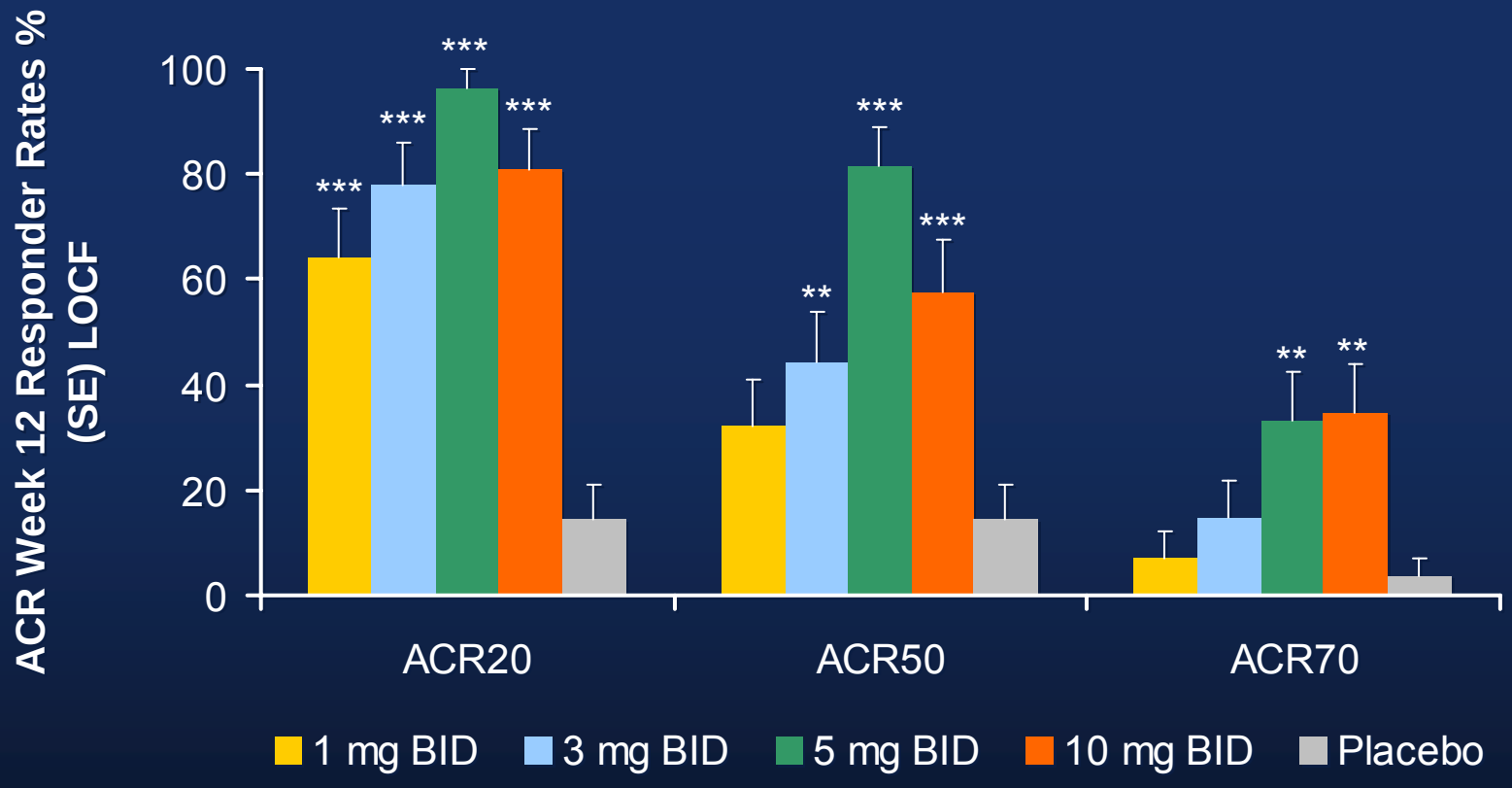
# Study 1039: Patient Disposition

| Dose | Treated | D / C | D / C | | |
|---|---|---|---|---|---|
| | | | AE† | AE Related to CP† | LOE† |
| 1 mg BID (n=28) | 28 | 2 (7.1) | 0 | 0 | 0 |
| 3 mg BID (n=28) | 27 | 4 (14.3) | 2 (7.4) | 1 (3.7) | 1 (3.7) |
| 5 mg BID (n=28) | 27 | 4 (14.3) | 4 (14.8) | 3 (11.1) | 0 |
| 10 mg BID (n=28) | 26 | 5 (17.9) | 4 (15.4) | 4 (15.4) | 0 |
| Placebo (n=28) | 28 | 5 (17.9) | 2 (7.1) | 2 (7.1) | 1 (3.6) |

Data are n (%); †data are % of treated patients

CP, CP-690,550; D / C, discontinuation; LOE, lack of efficacy; AE, adverse event

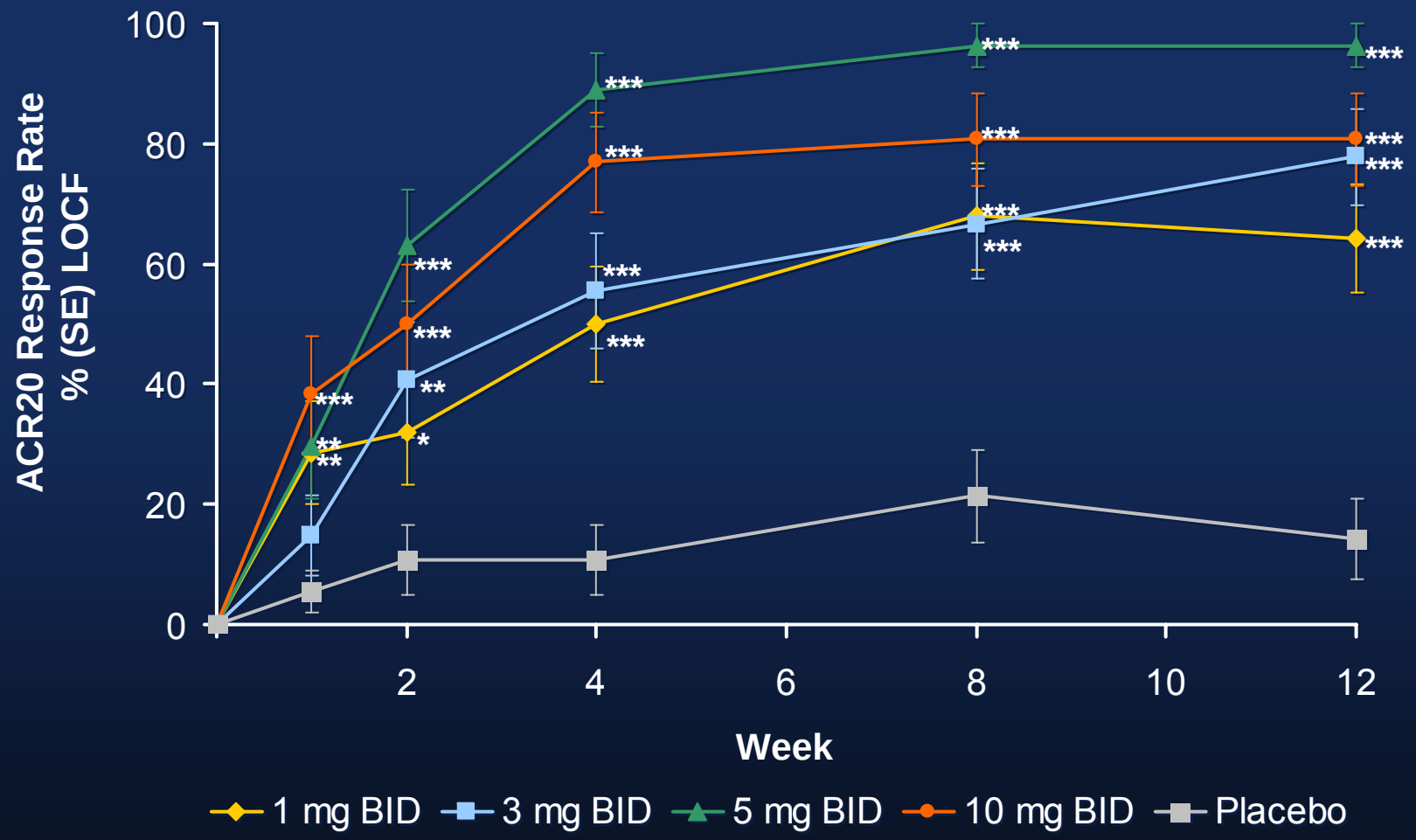
# Study 1039: Week 12 ACR Response Rates




Compared to placebo; **p≤0.01; ***p≤0.001

LOCF, last observation carried forward; SE, standard error

# Study 1039:
# Time Course of ACR20 Response



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# Study 1039:
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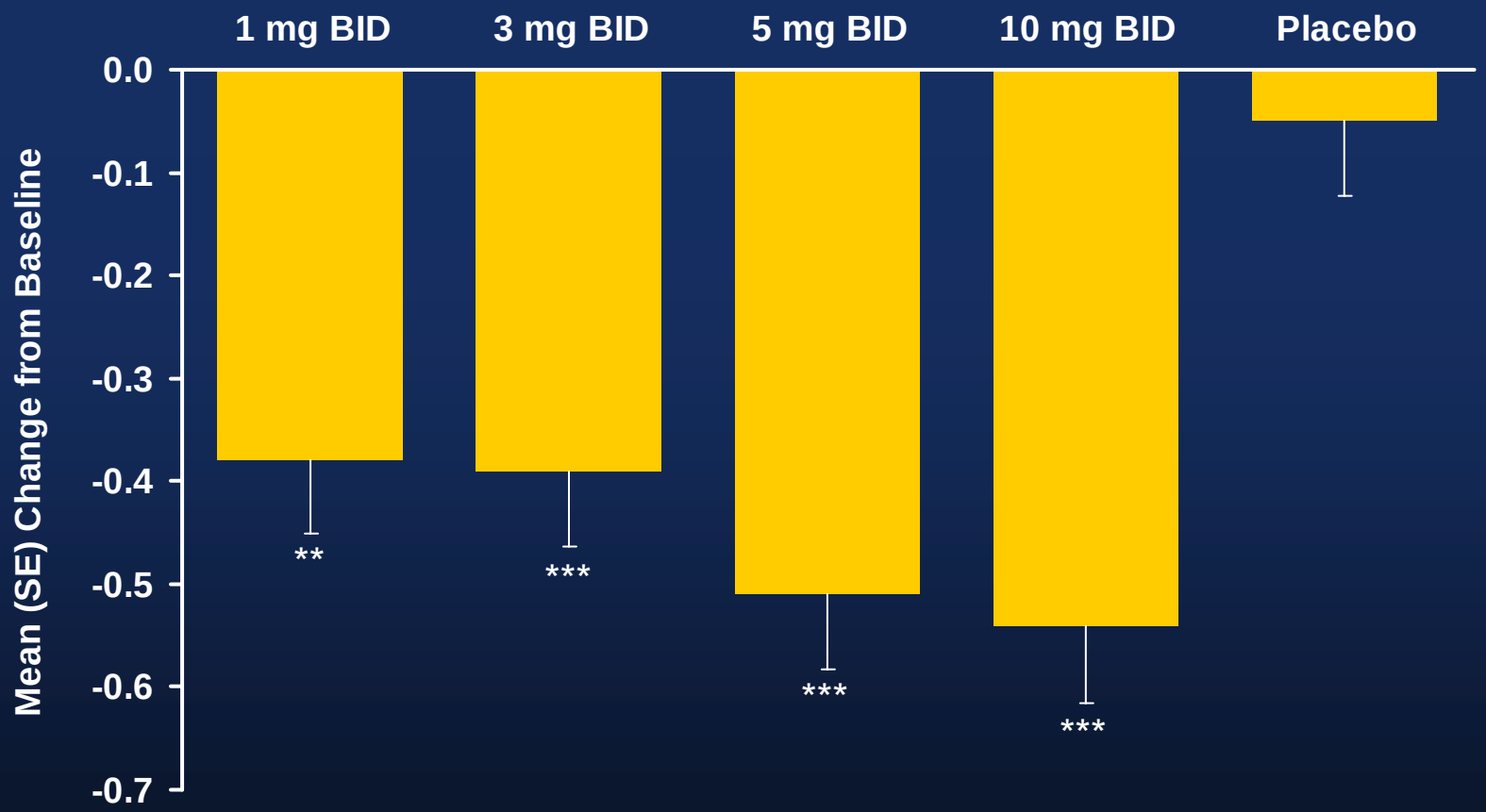





Compared to placebo *p≤0.05; **p≤0.01; ***p≤0.001

# Study 1039: Adverse Events Occurring in at Least 3 Patients in Any Arm, n (%)

| MedDRA | 1 mg BID N=28 | 3 mg BID N=27 | 5 mg BID N=27 | 10 mg BID N=26 | Placebo N=28 |
|---|---|---|---|---|---|
| **Gastrointestinal disorders** | **4 (14.3)** | **0** | **5 (18.5)** | **3 (11.5)** | **2 (7.1)** |
| Stomach discomfort | 0 | 0 | 3 (11.1) | 0 | 0 |
| **Infections and infestations** | **3 (10.7)** | **8 (29.6)** | **3 (11.1)** | **11 (42.3)** | **6 (21.4)** |
| Nasopharyngitis | 3 (10.7) | 1 (3.7) | 1 (3.7) | 4 (15.4) | 4 (14.3) |
| **Investigations** | **3 (10.7)** | **5 (18.5)** | **10 (37.0)** | **7 (26.9)** | **1 (3.6)** |
| ALT increased | 1 (3.6) | 2 (7.4) | 6 (22.2) | 2 (7.7) | 1 (3.6) |
| AST increased | 1 (3.6) | 2 (7.4) | 4 (14.8) | 1 (3.8) | 1 (3.6) |
| Blood cholesterol increased | 0 | 3 (11.1) | 1 (3.7) | 1 (3.8) | 0 |

Patients counted once per treatment in each row

ALT, alanine aminotransferase; AST, aspartate aminotransferase

# Study 1039: Incidence of Transaminase Elevations

| Dose (n) | ALT, n (%) | | | | AST, n (%) | | | |
|---|---|---|---|---|---|---|---|---|
| | Abnormal Baseline | >1x ULN | >2x ULN | >3x ULN | Abnormal Baseline | >1x ULN | >2x ULN | >3x ULN |
| 1 mg BID (28) | 1 (4) | 4 (15) | 1 (4) | **0** | 0 | 4 (14) | 0 | **0** |
| 3 mg BID (27) | 2 (8) | 3 (12) | 1 (4) | **0** | 0 | 2 (7) | 1 (4) | **0** |
| 5 mg BID (27) | 2 (8) | 6 (24) | 2 (8) | **2 (8)** | 0 | 6 (22) | 2 (7) | **0** |
| 10 mg BID (26) | 2 (8) | 7 (29) | 1 (4) | **1 (4)** | 2 (8) | 5 (21) | 1 (4) | **1 (4)** |
| Placebo (28) | 1 (4) | 3 (11) | 1 (4) | **0** | 2 (8) | 2 (8) | 1 (4) | **0** |

Patients allowed to enroll with AST / ALT ≤ 1.5 X ULN

Only patients with normal baseline values were included in the > 1 X, > 2 X and > 3 X tallies

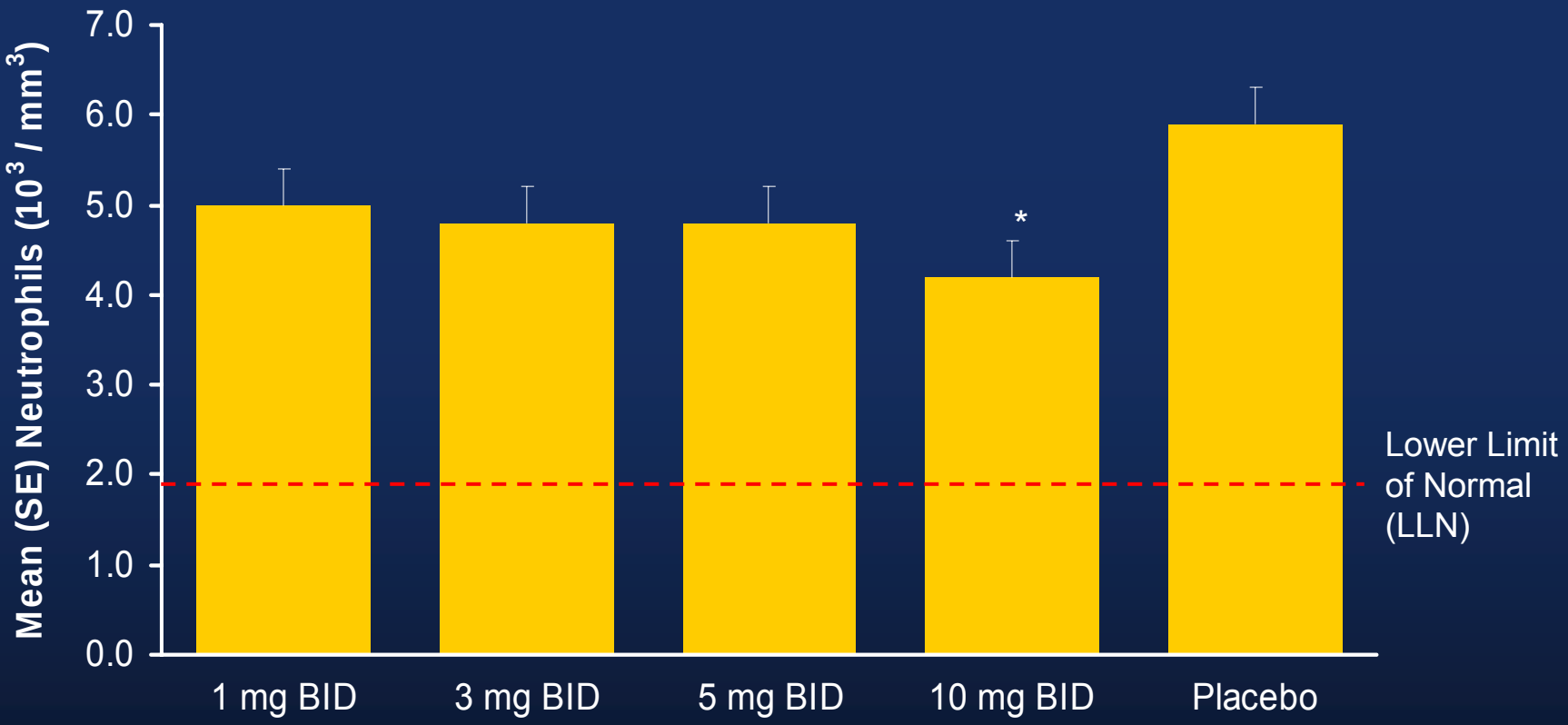
# Study 1039: Adverse Events That Led to Discontinuation From Treatment

| Dose | Adverse Event |
|---|---|
| 1 mg BID | – |
| 3 mg BID | ▶ **Osteoarthritis**<br>▶ ALT and AST increased |
| 5 mg BID | ▶ **Femur fracture**<br>▶ White blood cell count decreased<br>▶ ALT and AST increased (2 patients) |
| 10 mg BID | ▶ **Cardiac failure** and pneumonia<br>▶ **Dyspnoea**<br>▶ ALT and AST increased<br>▶ Peritonsillitis |
| Placebo | ▶ Gastroenteritis and upper respiratory tract infection<br>▶ Purpura |



Red indicates SAEs, or serious adverse events

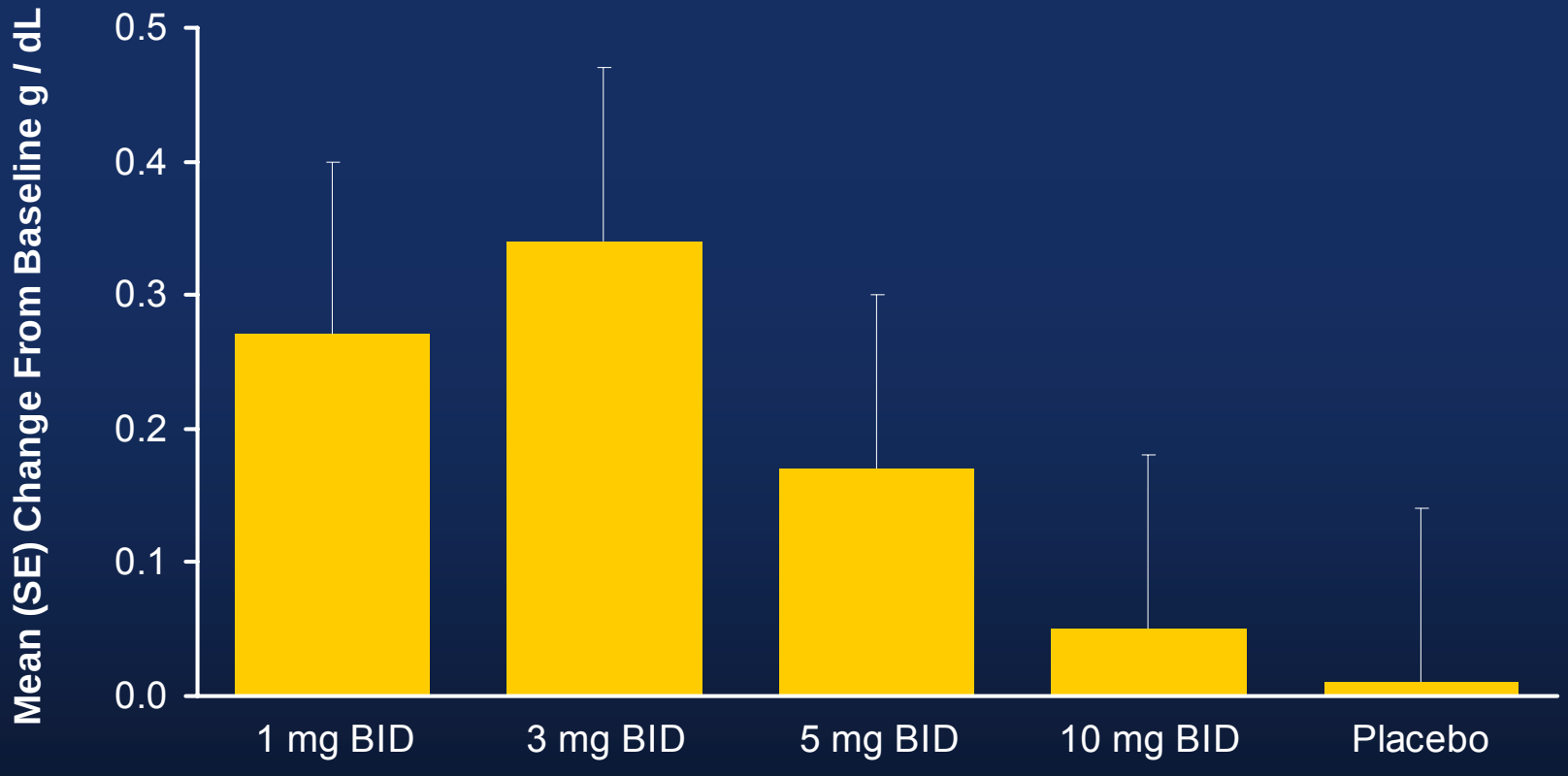
# Study 1039: Absolute Neutrophil Count






Compared to placebo *p≤0.05

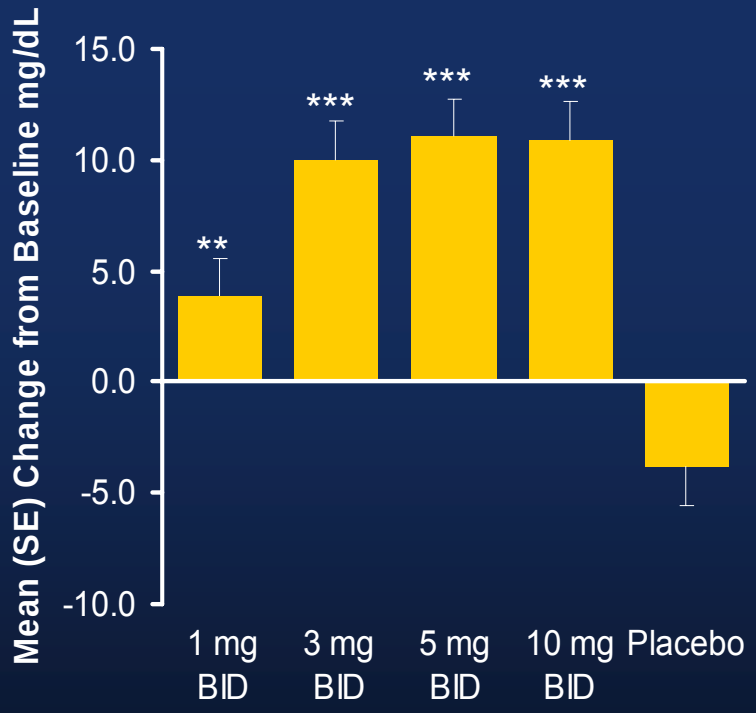
# Study 1039: Change in Hemoglobin



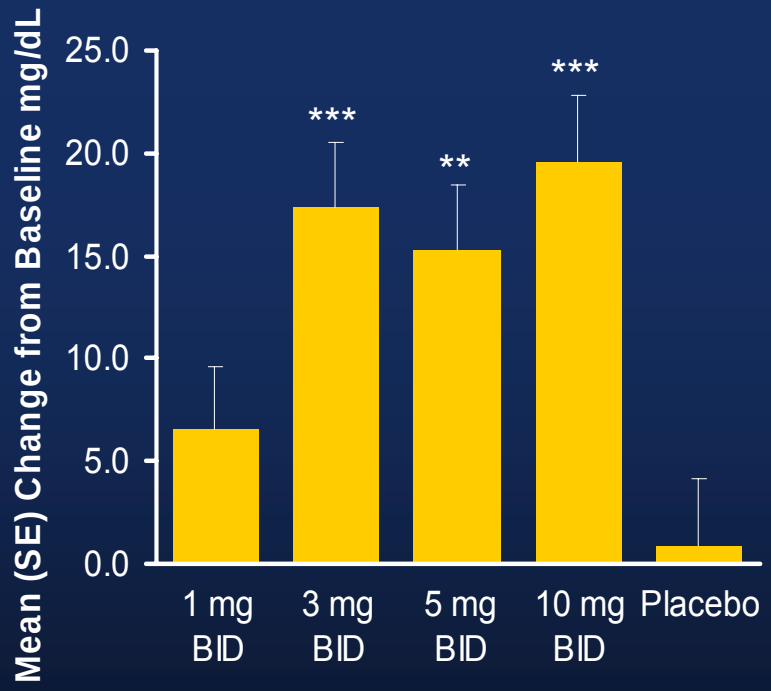

**No Significant Change in Hemoglobin**

# Study 1039:
# Change in HDL and LDL Cholesterol

## HDL




## LDL




**Dose Dependent Increases in HDL and LDL**

Compared to placebo *p≤0.05; **p≤0.01; ***p≤0.001

HDL, high density lipoprotein; LDL, low density lipoprotein

# Study 1039: Conclusions

- All CP-690,550 doses were efficacious vs. placebo
  - ACR20 response rates: all doses statistically significantly superior to placebo at Week 12
  - ACR50 response rates: all doses except 1 mg BID significantly superior to placebo at Week 12
  - ACR70 response rates: 5 mg BID and 10 mg BID significantly superior to placebo at Week 12
  - Significant difference relative to placebo was noted as early as 1 week after the start of therapy
- All CP-690,550 dose groups demonstrated significant differences relative to placebo in HAQ DI

# Study 1039: Conclusions (continued)

- CP-690,550 was generally well-tolerated
  - No serious infections or opportunistic infections
  - No significant decreases in hemoglobin
  - Dose-related decreases in mean absolute neutrophil counts
  - Dose-dependent increases in LDL and HDL cholesterol
  - ALT/AST increases of >3x ULN were noted in the 5 mg BID and 10 mg BID groups

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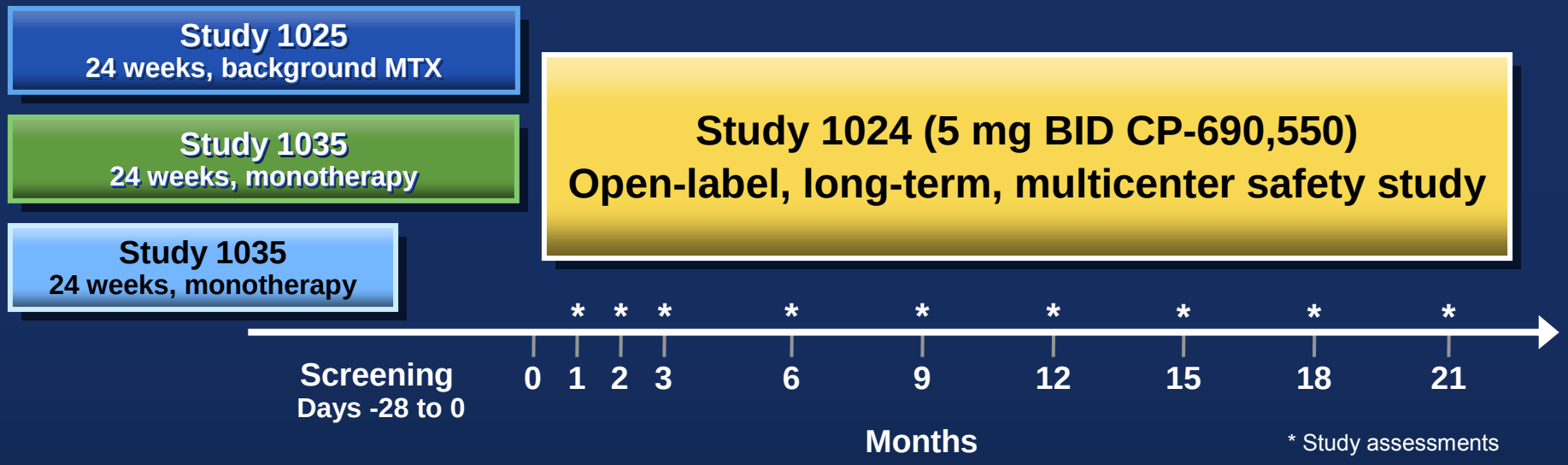
  - 12 week interim analysis of 6-month monotherapy study (Study 1035)
  - 12-week Japanese study on background MTX (Study 1039)
  - **Update on Open Label Extension study (Study 1024)**
- Summary and overview of Phase 3 Program

# Study 1024 Design




- Roll-over into Study 1024 ≤ 7 days after last study visit in Studies 1025 and 1035
- Patients from Study 1019 were off-study and were re-screened before entry
- Background RA therapy (including glucocorticoids and traditional DMARDs) allowed
- Specific rescue medications and adjustments to background therapy were allowed
- Permanent or temporary dose reductions were allowed for AEs
- Study approved by local IRBs / ECs; all patients gave written informed consent

# Study 1024: Interim Analysis

- Data from 655 patients, enrolled as of Dec 01, 2008
- At data cut-off, the number of patients completing treatment through 6 and 12 months was:
  - 446 patients: 6 months
  - 125 patients: 12 months
- Median duration of treatment was:
  - 161.0 days (range 1-658 days)
- Baseline definition
  - 1019 patients – 28 days prior to enrollment in 1024
  - 1025 and 1035 patients – baseline of index study

# Study 1024: Summary of Safety Data at Interim Analysis

- Most AEs mild to moderate in severity
  - 10 Severe AEs:
    - Acne, acute renal failure, diarrhea, disseminated tuberculosis*, diverticulitis*, herpes zoster*, pneumonia*, staphylococcal infection*, upper abdominal pain, urinary tract infection*
- 42 serious AEs reported in 26 patients
- 9 serious infections in 9 patients
  - 9 events/~255 patient years of exposure (~3.53/100 pt yrs)
- 2 deaths (both sudden)
  - 57 yr old white male with history of multiple cardiovascular co-morbidities
  - 70 yr old Hispanic female with a history of hypertension and epilepsy



* Infections rated as severe (n=6)

# Study 1024: Laboratory Data at Interim Analysis

| All Patients (Mean ± SD) | Baseline (n=635-646) | Month 6 (n=301-316) | Month 12 (n=56-59) |
|---|---|---|---|
| Neutrophil count, $10^3/mm^3$ | 5.72 ± 2.38 | 4.89 ± 1.95 | 4.64 ± 2.27 |
| Hemoglobin, g/dL | 13.05 ± 1.41 | 13.14 ± 1.27 | 12.96 ± 1.42 |
| LDL, mg/dL | 112.04 ± 34.46 | 129.54 ± 38.55 | 131.00 ± 37.89 |
| HDL, mg/dL | 56.27 ± 15.54 | 60.44 ± 17.82 | 61.69 ± 17.66 |

**Laboratory Changes are Similar to Those Seen in Short-Term Studies**



LDL, low density lipoprotein; HDL, high density lipoprotein

# Study 1024: Conclusions from Interim Analysis

- CP-690,550 was generally well-tolerated and had a similar safety profile compared to that observed in the randomized index studies

# CP-690,550 Update

- Compound overview and mechanism of action
- Overview of Phase 2 RA Program
- New presentations at EULAR
  - 12 week interim analysis of 6-month monotherapy study (Study 1035)
  - 12-week Japanese study on background MTX (Study 1039)
  - Update on Open Label Extension study (Study 1024)
- **Summary and overview of Phase 3 Program**

# CP-690,550
# RA Phase 2 Program Conclusions

- 4/4 studies achieved statistical significance on the primary endpoint (ACR20 Response)
- Extensive Phase 2 RA Program enrolled >1,000 patients and explored a CP-690,550 dose range of 1 to 30 mg BID
- CP-690,550 dosed ≥ 3 mg BID was generally efficacious, compared to placebo, as measured by:
  - ACR response rates
  - Changes from Baseline in the DAS and DAS remission rates
  - Improvements in patient reported outcome measures including HAQ DI
- Efficacy was seen early (within 2 weeks) when CP-690,550 was dosed either as monotherapy or on background MTX

# CP-690,550
# RA Phase 2 Program Conclusions

- Safety profile will continue to be monitored and further characterized throughout Phase 3 including:
  - Decreases in absolute neutrophil counts and hemoglobin
  - Increases in total, LDL and HDL cholesterol
  - Increases in transaminases
  - Infections
    - » Current rate of serious infections is ~4.5/100 patient-years
- Doses of 5 and 10 mg BID have been advanced into Phase 3



Pfizer

# Phase 3 Clinical Studies Enrolling

| Study # | Patient Population | Objectives | Number of Subjects | CP-690,550 Dosage | Duration | Control / Active Comp |
|---|---|---|---|---|---|---|
| A3921044 | Inadequate response to bkgd MTX | Signs & Symptoms Structure Physical Fxn | 750 | 5 mg BID 10 mg BID | 24 months | Placebo |
| A3921045 | Monotherapy | Signs & Symptoms Physical Fxn | 500 | 5 mg BID 10 mg BID | 6 months | Placebo |
| A3921046 | Inadequate response to bkgd DMARDs | Signs & Symptoms Physical Fxn | 750 | 5 mg BID 10 mg BID | 12 months | Placebo |
| A3921064 | Inadequate response to bkgd MTX | Signs & Symptoms Physical Fxn | 700 | 5 mg BID 10 mg BID | 12 months | Placebo / Humira® 40 mg s.c. EOW |

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

- CP-690,550 is the first Janus Kinase inhibitor, a novel immune pathway mechanism that has the potential to treat patients with RA as well as a number of other autoimmune diseases
- If successful, CP-690,550 could be the first new oral DMARD to be marketed in more than 10 years


# Thank You

## Questions?

# CP-690,550 Update

## EULAR 2009