Disclosure of Conflicts of Interest

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[JNJ-77242113 Treatment Induces a Strong Systemic Pharmacodynamic Response Versus Placebo in Serum Samples of Patients With Plaque Psoriasis: Results From the Phase 2, FRONTIER 1 Study]

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Disclosure of Conflicts of Interest

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▪ **A. Kannan, D. Strawn, D. Horowitz, S. Bhagat, D. Richards, D. Ruane, B. McRae, M.C. Holland, L. Miller, M. Miller, and C. DeKlotz** are employees of Janssen Research & Development, LLC, and **Y.-W. Yang** is an employee of Immunology Global Medical Affairs, Janssen Pharmaceutical Companies of Johnson & Johnson; employees may own stock/stock options in Johnson & Johnson, of which Janssen is a subsidiary.

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JNJ-77242113 Treatment Induces a Strong Systemic Pharmacodynamic Response Versus Placebo in Serum Samples of Patients With Plaque Psoriasis: Results From the Phase 2, FRONTIER 1 Study

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Background/Objective

- JNJ-77242113, an orally administered interleukin-23 receptor (IL-23R) antagonist peptide, demonstrated significantly greater efficacy compared with placebo (PBO) in adults with moderate-to-severe plaque psoriasis in the phase 2, FRONTIER 1 study (NCT05223868)
- Clinically validated therapeutics that target the IL-23 pathway in psoriasis drive systemic pharmacodynamic (PD) changes in the serum levels of beta-defensin 2 (BD-2), IL-22, IL-17A, and IL-17F relative to baseline
- In this analysis, we evaluated the PD response to JNJ-77242113 and its relationship to clinical efficacy

Pinter A, et al. EADV Congress; October 11-14, 2023; Berlin, Germany.
Methods

- FRONTIER 1 was a randomized, double-blind, PBO-controlled, dose-ranging, phase 2 study of JNJ-77242113 in the treatment of moderate-to-severe plaque psoriasis.

- Patients were randomized 1:1:1:1:1:1 to receive JNJ-77242113 25 mg QD, 25 mg BID, 50 mg QD, 100 mg QD, 100 mg BID, or PBO through Week 16.

- Serum levels of psoriasis disease biomarkers BD-2, IL-22, IL-17A, and IL-17F relative to baseline were analyzed in FRONTIER 1 patients who received PBO or JNJ-77242113 and compared to clinical response.

- A linear mixed effect model was used to analyze the treatment over time interaction, baseline serum protein levels, and patient random effect.

BID=Twice daily; LTE=Long-term extension; QD=Once daily.

Pinter A, et al. EADV Congress; October 11-14, 2023; Berlin, Germany.
JNJ-77242113 PD response is significantly distinguished from placebo at all doses

Significant dampening of serum BD-2, higher reduction observed with 100 mg BID

• Fold reduction of BD-2 by all JNJ-77242113 doses is statistically significant relative to placebo starting from Week 4
• Fold reduction of BD-2 over time with 100 mg BID dose was statistically significant relative to all other doses of JNJ-77242113 starting from Week 8

*nominal p<0.05 for all doses vs placebo starting from Week 4; †nominal p<0.05 for 100 mg BID vs other active dose arms at that time point. Linear mixed effect model accounts for treatment*time interaction, baseline serum protein levels, and subject random effect. Plots track mean values (estimated marginal means); error bars are model-based 95% confidence intervals.

Pinter A, et al. EADV Congress; October 11-14, 2023; Berlin, Germany.
JNJ-77242113 PD response robustly correlates with clinical outcomes

Strong correlation observed between dampening of serum BD-2 and PASI response

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JNJ-77242113 PD response is significantly distinguished from placebo at all doses

Significant dampening of serum IL-22, higher reduction observed with 100 mg BID

- Fold reduction of IL-22 by all JNJ-77242113 doses is statistically significant relative to placebo starting from Week 4
- Fold reduction of IL-22 over time with 100 mg BID dose was statistically significant relative to all other doses of JNJ-77242113 starting from Week 12

*nominal p<0.05 for all doses vs placebo starting from Week 4; †nominal p<0.05 for 100 mg BID vs other active dose arms at that time point. Linear mixed effect model accounts for treatment*time interaction, baseline serum protein levels, and subject random effect. Plots track mean values (estimated marginal means); error bars are model-based 95% confidence intervals.

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JNJ-77242113 PD response robustly correlates with clinical outcomes
Strong correlation observed between dampening of serum IL-22 and PASI response

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JNJ-77242113 PD response is significantly distinguished from placebo at all doses

Significant dampening of serum IL-17A and IL-17F, higher reduction observed with 100 mg BID

- Fold reduction of IL-17A and IL-17F by all JNJ-77242113 doses is statistically significant relative to placebo
- Fold reduction of IL-17A and IL-17F over time with 100 mg BID dose was numerically lower relative to all other doses of JNJ-77242113 starting from Week 8

*nominal p<0.05 for all doses vs placebo; †nominal p<0.05 for 100 mg BID vs other active dose arms at that time point. Linear mixed effect model accounts for treatment*time interaction, baseline serum protein levels, and subject random effect. Plots track mean values (estimated marginal means); error bars are model-based 95% confidence intervals.

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JNJ-77242113 treatment did not increase serum levels of IL-23 in psoriasis patients

Box plots are median and interquartile range (IQR).

Pinter A, et al. EADV Congress; October 11-14, 2023; Berlin, Germany.
Conclusions

▪ We show for the first time that specific targeting of the IL-23 pathway through inhibition of IL-23R signaling with the novel oral IL-23 receptor antagonist JNJ-77242113 induces a strong systemic PD response in psoriasis patients that is significantly distinguished from PBO

▪ We provide evidence supporting that the JNJ-77242113 PD response corroborates the observed clinical efficacy of JNJ-77242113

▪ Importantly, JNJ-77242113 treatment did not increase serum levels of IL-23 in psoriasis patients

▪ Taken together, consistent with its mechanism of action, JNJ-77242113 dampens objective biomarkers of IL-23 pathway activation and psoriasis disease severity to drive disease improvement