# Sustained Improvements in Psoriasis Area and Severity Index and in Percent Body Surface Area of Psoriasis With JNJ-77242113 in Patients With Moderate-to-Severe Plaque Psoriasis: Treat-to-Target Analyses in the FRONTIER 1 & 2 Studies


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## Key Takeaways

- **Treatment with JNJ-2113 provided robust and sustained skin improvements, consistent with achievement of important treatment targets, in patients with moderate-to-severe PsO**
- **The highest levels of improvement and response rates were observed with JNJ-2113 100 mg BID, with two-thirds of patients achieving PASI ≤2 or BSA ≤3% and approximately half achieving PASI ≤1 or BSA ≤1% at W16**
- **Patient- and group-level data indicated maintenance of JNJ-2113 stringent response through W52**

## Background

- Defined thresholds for Psoriasis Area and Severity Index (PASI) and psoriatic body surface area (BSA) are relevant disease endpoints that inform treat-to-target (T2T) management strategies in psoriasis (PsO)[1,2]
- Interleukin (IL)-23 pathway inhibition via monoclonal antibodies has demonstrated efficacy and safety in patients with moderate-to-severe PsO[3]
- Currently, no oral therapies selectively target the IL-23 pathway

**JNJ-77242113 (JNJ-2113)**

- First and only targeted oral peptide that inhibits IL-23 signaling by binding to the IL-23 receptor
- Showed superior clinical efficacy vs placebo (PBO) in the phase 2 FRONTIER 1 study, which was durable through 1 year of the FRONTIER 2 long-term extension (LTE) study, in patients with moderate-to-severe plaque PsO[4,5]

## Objectives

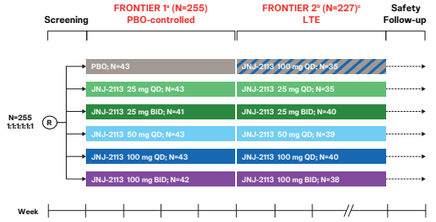
**To assess the effect of JNJ-2113 on the achievement of defined treatment goals in patients with moderate-to-severe plaque PsO through 1 year in FRONTIER 1 and 2**

## Methods

### FRONTIER 1 & FRONTIER 2 Study Designs

**Key inclusion criteria:**

- Moderate-to-severe plaque PsO
  - ≥18 years old
  - PASI ≥12
  - IGA ≥3
  - BSA ≥10%
- Diagnosed with PsO, with or without psoriatic arthritis, for ≥6 months
- Candidate for phototherapy or systemic therapy




[a]NCT05223866. [b]NCT05364554. [c]At W16, 227 participants from FRONTIER 1 entered FRONTIER 2 LTE study. [d]Final safety follow-up for participants who did not enter the LTE. Those not participating in the LTE completed 4 weeks of safety follow-up to complete the FRONTIER 1 study. BID=Twice daily; BSA=Body surface area; IGA=Investigator's Global Assessment; LTE=long-term extension; PASI=Psoriasis Area and Severity Index; PBO=Placebo; PsO=Psoriasis; QD=Once daily; R=Randomization; W=Week.

### Assessments & Analyses

**Percent change from baseline in the PASI score through W52**

**The PASI assesses PsO severity based on three PsO symptoms (erythema, induration, and desquamation)[6]**

- Least squares (LS) means and p-values are based on mixed models for repeated measures (MMRM) with treatment group, visit, treatment group-by-visit interaction, baseline weight category (≤90 kg, >90 kg), baseline weight category-by-visit interaction, baseline PASI total score, and baseline PASI total score-by-visit interaction as covariates
- Patients who discontinued study agent due to lack of efficacy, worsening of PsO, or initiation of a prohibited PsO treatment were considered to have zero change from baseline after the occurrence
- Missing data were handled by MMRM under missing at random assumption

**Achievement of PASI and BSA treatment targets through W52**

**Absolute PASI thresholds of ≤5, ≤3, ≤2, ≤1, and 0**

- PASI ≤5, ≤3, and ≤2 represent moderate disease control
- PASI ≤2 is a relevant T2T endpoint in the clinical setting[7]
- PASI ≤1 and 0 represent stringent disease control

**PsO BSA thresholds of ≤3% and ≤1%**

- BSA ≤3% represents acceptable response at W12 of treatment[7]
- BSA ≤1% represents a target response at W12 of treatment[7]

**JNJ-2113 vs PBO at W12 and/or W16:** Cochran-Mantel-Haenszel chi-square test stratified by baseline weight (≤90 kg vs >90 kg); nominal p-values

**Nonresponder imputation (NRI):**

- Patients who discontinued study agent due to lack of efficacy, worsening of PsO, or initiation of a prohibited PsO treatment were considered nonresponders after the occurrence
- Remaining patients with missing data were considered nonresponders

Among PBO-randomized patients, only those who crossed over from PBO to JNJ-2113 (PBO→100 mg QD) were included beyond W16

## Results

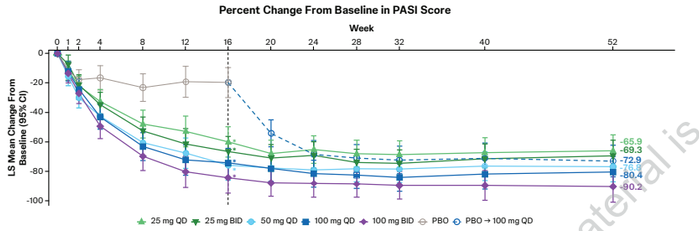
### *FRONTIER 1 participants had established, moderate-to-severe plaque PsO*

| | | PBO (N=43) | JNJ-2113 25 mg QD (N=43) | JNJ-2113 25 mg BID (N=41) | JNJ-2113 50 mg QD (N=43) | JNJ-2113 100 mg QD (N=43) | JNJ-2113 100 mg BID (N=42) | JNJ-2113 All (N=212) | All Groups (N=255) |
|---|---|---|---|---|---|---|---|---|---|
| **Demographics** | | | | | | | | | |
| | Age, years | 43.9 (14.7) | 44.5 (12.7) | 45.7 (11.9) | 45.1 (11.1) | 44.7 (14.1) | 42.0 (11.3) | 44.4 (12.2) | 44.3 (12.6) |
| | Female | 42% | 26% | 27% | 37% | 26% | 29% | 29% | 31% |
| | White/Asian | 86%/12% | 70%/28% | 66%/17% | 72%/21% | 81%/16% | 71%/21% | 72%/21% | 74%/19% |
| | Weight, kg | 92.1 (24.7) | 89.0 (19.4) | 90.8 (22.1) | 87.6 (19.2) | 85.4 (22.5) | 88.5 (16.9) | 88.2 (20.0) | 88.9 (20.9) |
| **Characteristics** | | | | | | | | | |
| | PsO disease duration, years | 17.9 (14.4) | 15.5 (11.8) | 18.1 (11.8) | 21.5 (11.2) | 19.5 (13.3) | 16.7 (13.8) | 18.3 (12.5) | 18.2 (12.8) |
| | PASI (0-72) | 19.0 (5.3) | 18.9 (5.3) | 18.5 (5.8) | 19.2 (5.1) | 18.4 (6.9) | 20.3 (6.5) | 19.1 (5.9) | 19.0 (5.8) |
| | Psoriatic BSA, % | 26.1 (15.7) | 21.1 (9.3) | 20.9 (11.9) | 23.9 (13.6) | 20.5 (13.7) | 24.2 (12.6) | 22.1 (12.3) | 22.8 (13.0) |
| | IGA | | | | | | | | |
| | Moderate (3)/Severe (4) | 88%/12% | 70%/30% | 80%/20% | 84%/16% | 81%/19% | 71%/29% | 77%/23% | 79%/21% |
| **Medication use at baseline** | | | | | | | | | |
| | Phototherapy[a] | 44% | 40% | 37% | 56% | 49% | 33% | 43% | 43% |
| | Biologics[b] | 16% | 16% | 32% | 26% | 21% | 21% | 23% | 22% |
| | Systemics[c] | 79% | 77% | 80% | 81% | 79% | 74% | 78% | 78% |

*Data shown are mean (SD) or percentage, unless otherwise indicated.* [a]Includes PUVA or UVB. [b]Includes etanercept, infliximab, adalimumab, ustekinumab, briakinumab, secukinumab, ixekizumab, brodalumab, guselkumab, risankizumab, tildrakizumab, alefacept, efalizumab, natalizumab, certolizumab pegol. [c]Includes conventional nonbiologic systemic therapies, novel nonbiologic systemic therapies, 1,25-vitamin D3 and analogs, phototherapy, and biologics. BID=Twice daily; BSA=Body surface area; IGA=Investigator's Global Assessment; JNJ-2113=JNJ-77242113; PASI=Psoriasis Area and Severity Index; PBO=Placebo; PsO=Psoriasis; PUVA=Psoralen plus ultraviolet A; SD=Standard deviation; QD=Once daily; UVB=Ultraviolet B.

### *Percent improvements in PASI score were greater with JNJ-2113 than PBO as early as W4, with continued and sustained improvement over time*

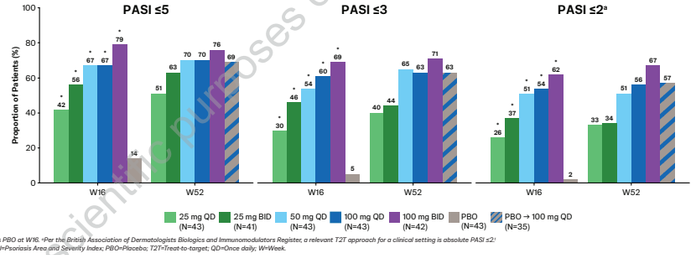
- Highest mean percent improvements in PASI score were seen with JNJ-2113 100 mg BID, with approximately 90% improvement at W52




*[a]All nominal p<0.001 vs PBO at W16. Dotted line indicates transition from PBO-controlled FRONTIER 1 to FRONTIER 2 LTE with PBO→100 mg QD. BID=Twice daily; CI=Confidence interval; LS=Least square; PASI=Psoriasis Area and Severity Index; PBO=Placebo; QD=Once daily; W=Week.*

### *Greater proportions of patients treated with JNJ-2113 vs PBO achieved absolute PASI thresholds of ≤5, ≤3, and ≤2 at W16; rates were maintained at W52*

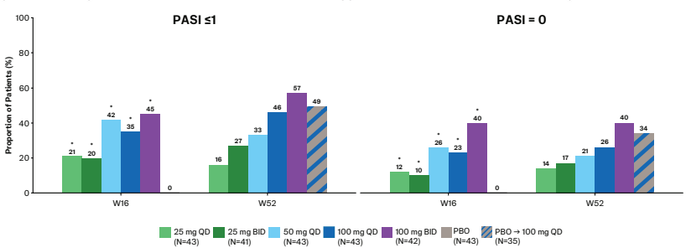
- 67% of patients receiving JNJ-2113 100 mg twice daily (BID) achieved PASI ≤2 at W52, a clinically relevant T2T threshold
- Response rates at W52 following PBO→100 mg once daily (QD) reached those with JNJ-2113 100 mg QD across absolute PASI thresholds




*[a]All nominal p<0.01 vs PBO at W16. [b]Per the British Association of Dermatologists Biologics and Immunomodulators Register, a relevant T2T approach for a clinical setting is absolute PASI ≤2[7]. BID=Twice daily; PASI=Psoriasis Area and Severity Index; PBO=Placebo; T2T=Treat-to-target; QD=Once daily; W=Week.*

### *Greater proportions of patients treated with JNJ-2113 vs PBO achieved stringent PASI thresholds of ≤1 and 0 at W16; rates were maintained or increased at W52*

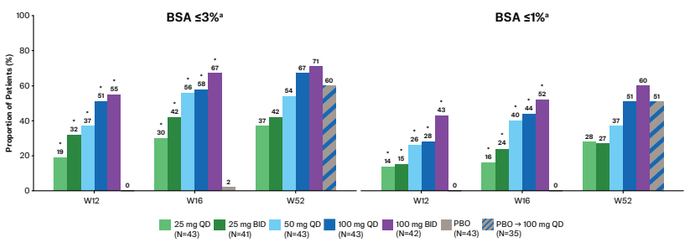
- 45% and 40% of patients receiving JNJ-2113 100 mg BID achieved PASI ≤1 and PASI=0, respectively, at W16
- Following PBO→100 mg QD, W52 rates for both PASI thresholds approached those with JNJ-2113 100 mg BID




*[a]Nominal p<0.05 to <0.01 vs PBO at W16. BID=Twice daily; PASI=Psoriasis Area and Severity Index; PBO=Placebo; QD=Once daily; W=Week.*

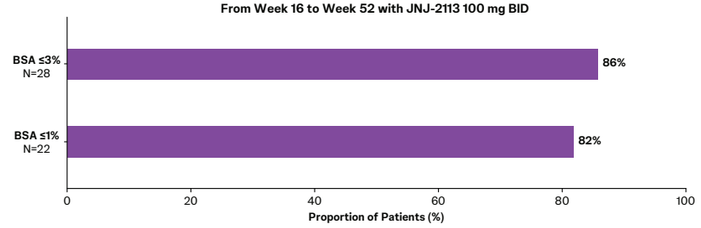
### *Greater proportions of patients treated with JNJ-2113 vs PBO achieved PsO BSA thresholds of ≤3% and ≤1% at W12 and W16; rates were maintained or increased at W52*

- At W52, 71% and 60% of patients treated with 100 mg BID achieved acceptable (≤3%) and target (≤1%) BSA responses, respectively
- Rates for both BSA thresholds at W52 following PBO→100 mg QD approached those with JNJ-2113 100 mg QD




*[a]All nominal p≤0.01 vs PBO at W16. [b]Per the National Psoriasis Foundation, at W12 (3 months) after treatment initiation, an acceptable response is BSA ≤3% and a target response is ≤1%[7]. BID=Twice daily; BSA=Body surface area; PBO=Placebo; QD=Once daily; W=Week.*

### *86% and 82% of patients treated with 100 mg BID achieving BSA ≤3% and ≤1% at W16, respectively, maintained response at W52*




*BID=Twice daily; BSA=Body surface area.*




**PRESENTED AT:** Maui Derm Hawaii 2025, Maui, Hawaii, USA; January 20-24, 2025. **REFERENCES: 1.** Mahil, SK. *Br J Dermatol.* 2020;182:1158-66. **2.** Armstrong, AW. *J Am Acad Dermatol.* 2017;76:290-8. **3.** Yu, A. *Expert Opin Biol Ther.* 2022;22:1489-1502. **4.** Bissonnette, R. *N Engl J Med.* 2024;390:510-21. **5.** Ferris, LK. Oral presentation 58758. AAD Annual Meeting; March 8-12, 2024; San Diego, CA, USA. **6.** Fredriksson, T. *Dermatologica.* 1978;157:238-44. **ACKNOWLEDGMENTS:** Layout design and reformatting for this encore presentation was provided by Sandeep Chavan of SIRO Medical Writing Pvt Ltd, Thane, India. Medical writing support was provided by JSS Medical Research, Inc, under the direction of the authors in accordance with Good Publication Practice guidelines (*Ann Intern Med.* 2022;176:1298-304). Sponsored by Janssen Research & Development, LLC, a Johnson & Johnson Company. **DISCLOSURES: KAP:** Clinical research grants, honoraria, and/or consultant, scientific advisor, investigator, speaker, and/or medical officer: AbbVie, Acelyrin, Aerie, Alumis, Amgen, Arcutis, Bausch Health/Valeant, Boehringer Ingelheim, Bristol Myers Squibb, Can-Fite Biopharma, Celltrion, Concert Pharmaceuticals, Dermavant, Dermira, Dice Pharmaceuticals, Dice Therapeutics, Eli Lilly, Exelo Biosciences, Forbion, Galderma, Horizon Therapeutics, Incyte, Janssen, Kymab, Kyowa Hakko Kirin, Leo Pharma, Meiji Seika Pharma, Mitsubishi Pharma, Nimbus Therapeutics, Novartis, Pfizer, Roivtone, Sanofi-Aventis/Genzyme, Sandoz, Sun Pharma, Takeda, Tanus Pharmaceuticals, Inc., UCB, Zai Lab Co., Ltd. **LKF:** Investigator: AbbVie, Acelyrin, Amgen, Apogee, Arcutis, Aristea, Boehringer Ingelheim, Bristol Myers Squibb, Cara Therapeutics, Castle Biosciences, DermTech, Eli Lilly, Galderma, GRAIL, Incyte, Janssen, Leo Pharma, Moberg, Mobius, Novartis, Regeneron, SkinAnalytics, Takeda, UCB, Consultant: AbbVie, Amgen, Apogee, Arcutis, Boehringer Ingelheim, Bristol Myers Squibb, Cara Therapeutics, Dermavant, DermTech, Janssen, Leo Pharma, Novartis, Pfizer, Regeneron, Takeda; Speaker: AbbVie, Arcutis, Boehringer Ingelheim, Bristol Myers Squibb, Regeneron. **AP:** Advisor and/or received speaker's honoraria and/or received grants and/or participated in clinical trials: AbbVie, Almirall Hermal, Amgen, Biogen Idec, BioNTech, Boehringer Ingelheim, Celgene, Celltrion, Eli Lilly, Galderma, GSK, Hexal, Janssen-Cilag GmbH, Klinge Pharma, Leo Pharma, MC2, Medac, Merck Serono, Mitsubishi, MSD, Novartis, Pascoe, Pfizer, Regeneron, Roche, Sandoz Biopharmaceuticals, Sanofi Genzyme, Schering-Plough, Tigercat Pharma, UCB Pharma, and Zyelig Pharma. **PB:** Principal investigator: AbbVie, Acelyrin, Air Liquide, Alkahest, Amgen, Arcutis, Asian, Atacama, Bristol, Bristol Myers Squibb, Dermavant, Dermira, Dung-A, Eli Lilly, Galderma, Hallux, Incyte, Janssen, Leo Pharma, Moberg, Ortho, Pfizer, Sun, Technoderma, UCB. Advisory Board: Cara, Ortho Dermatologics, Bristol Myers Squibb, La Roche Posay; Consulting: Bristol Myers Squibb, Hesma. **RBV:** Grants/research support and/or speakers bureau/honoraria and/or consulting fees: AbbVie, Actelion, Amgen, Aralez, Arcutis, Bausch Health, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Centocor, Cipher, Dermira, Dermavant, Galderma, GSK, Innoaderm, Janssen, Kabi-Care, Leo Pharma, Lilly, Meiji, Merck, Novartis, Pfizer, Regeneron, Sandoz, Sun, Takeda, UCB, Vatris-Mylan. **AEP:** Investigator, advisor and/or speaker and/or received educational support from AbbVie, Almirall, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Galderma, Janssen, Leo Pharma, Lilly, Novartis, Pfizer, Sanofi, UCB. **TO, Y-KS, SL, AMD:** Employees of Janssen Research & Development, LLC; employees may own stock/stock options in Johnson & Johnson. **Y-WY:** Employee of Janssen Pharmaceutical Companies of Johnson & Johnson; employees may own stock/stock options in Johnson & Johnson. **RB:** Advisory board member, consultant, speaker and/or investigator and received honoraria and/or grants: AbbVie, Alumis, Amgen, Arcutis, Bausch Health, Boston, Bristol Myers Squibb/Celgene, Dermavant, Eli Lilly, Janssen, Leo Pharma, Nimbus, Novartis, Pfizer, Regeneron, UCB, Ventyxbio and Xencor; also an employee and shareholder of Innovaderm Research. PREVIOUSLY PRESENTED AT EADV Congress 2024; Amsterdam, the Netherlands; September 25-28, 2024.