# Phase 3 Results From an Innovative Trial Design of Treating Plaque Psoriasis Involving Difficult-to-Treat, High-Impact Sites With Icotrokinra, a Targeted Oral Peptide That Selectively Inhibits the IL-23–Receptor

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## Background



#### Icotrokinra for plaque psoriasis

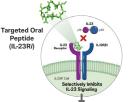
- Patients with moderate-to-severe plaque psoriasis (PsO) are generally limited to injectable therapies to achieve high-level efficacy with a favorable safety profile
- Icotrokinra (ICO) is a first-in-class targeted oral peptide that:
- Selectively binds the interleukin (IL)-23 receptor and inhibits IL-23 pathway signaling<sup>1</sup>
- Demonstrated significant skin clearance and no safety signals through 1 year in phase 2 PsO studies<sup>23</sup> and through Week (W)24 in adults and adolescents with moderate-to-severe plaque PsO in the phase 3 ICONIC-LEAD study\*

## **Objectives**



The pivotal, phase 3 ICONIC-TOTAL study evaluated ICO in adults and adolescents with plaque PsO involving difficult-to-treat, high-impact sites, by employing a novel basket-like design; key clinical/patient-reported outcomes (PROs) and safety-related findings are reported through W16

# Icotrokinra Blocks IL-23 From Binding to its Receptor



Inhibits IL-17A, IL-17F, IL-22, and IFN<sub>Y</sub> Production

IFN-interferon, IL-12R)1-interleukin-12 receptor beta 1, IL-17A-interleukin-1/A IL-17F-interleukin-17F, IL-22-interleukin-22, IL-23-interleukin-23, IL-23R-interleukin-23 receptor, IL-23R-interleukin-23 receptor inhibitor.

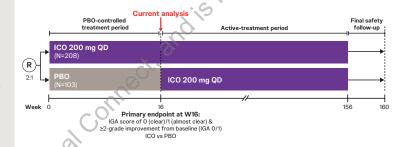
## ICONIC-TOTAL: a novel basket-like design

Adults and adolescents with plaque PsO involving high-impact sites evaluated using a basket-like study design (N=311)



### Key inclusion criteria

- ≥12 years
- Plaque PsO for ≥26 weeks
- Body surface area (BSA) ≥1% and Investigator's Global Assessment (IGA) score ≥2
- At least moderate high-impact PsO involving ≥1 site:
- Scalp PsO: scalp-specific IGA (ss-IGA) score ≥3
- Genital PsO: static Physician's Global Assessment of Genitalia (sPGA-G) score ≥3
- Hand/foot PsO: Physician's Global Assessment of hands and feet (hf-PGA) score ≥3
- Candidate for phototherapy or systemic treatment for plaque PsO and failed ≥1 topical



((c)) with the following intercurrent events, nonresponder imputation was applied to pts with missing data. All-ordware event, (C)-circlwin, (A4-investigation flow) and continued a nonresponder imputation was applied to pts with missing data. All-ordware event, (C)-circlwin, (A4-investigation flow) and continued a nonresponder imputation was applied to pts with missing data. All-ordware event, (C)-circlwin, (A4-investigation flow) and continued a nonresponder imputation was applied to pts with missing data. All-ordware event, (C)-circlwin, (A4-investigation flow) and continued in the following inforcurrent events, nonresponder imputation was applied to pts with missing data. All-ordware event, (C)-circlwin, (A4-investigation flow) and continued in the following inforcurrent events, nonresponder imputation was applied to pts with missing data. All-ordware event, (C)-circlwin, (A4-investigation flow) and continued in the following inforcurrent events, nonresponder imputation was applied to pts with missing data. All-ordware event, (C)-circlwin, (A4-investigation flow) and continued in the following inforcurrent events, nonresponder imputation was applied to pts with missing data. All-ordware event, (C)-circlwin, (A4-investigation flow) and continued in the following inforcurrent events, nonresponder imputation was applied to pts with missing data. All ordware events (C)-circlwin, (A4-investigation flow) and (C)-circlwin, (A4-investigati

## **Key Takeaways**



In ICONIC-TOTAL, a pivotal phase 3 study evaluating ICO in a diverse cohort of pts with plaque PsO and difficult-to-treat, high-impact site involvement:

- ICO demonstrated significantly higher rates of clear/almost clear skin, including in the scalp and genital areas, than PBO at W16
- ICO-treated pts achieved significantly higher PRO response rates, including meaningful improvements in the scalp and genital areas, vs PBO at W16
- Rates of AEs were generally similar in the ICO and PBO groups; no safety signal was identified through W16

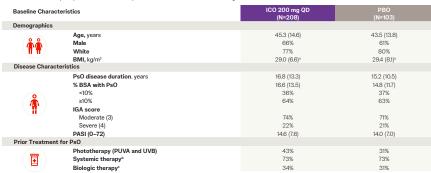


ICONIC-TOTAL results complement those of the ongoing phase 3 ICONIC-LEAD study evaluating ICO in adults and adolescents with moderate-to-severe plaque PsO<sup>4</sup>

## Results

#### Baseline characteristics were generally similar between groups

Overall, 5% of pts (ICO: 4%; PBO: 9%) discontinued treatment through W16<sup>d</sup>



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#### Scalp and genital PsO severity at baseline was generally similar between groups

 Among the limited subset of pts with hf-PGA score ≥3, a higher proportion in the ICO group had severe involvement vs PBO

Severe involvement vs F DO				
High-impact Site PsO Severity		ICO 200 mg QD (N=208)	PBO (N=103)	
	ss-IGA score ≥3	167 (80%)	85 (83%)	
	Moderate (3)	80%	75%	
17	Severe (4)	20%	25%	
	sPGA-G score ≥3	98 (47%)	42 (41%)	
o Q	Moderate (3)	77%	69%	
	Severe (4)	22%	29%	
	Very severe (5)	1%	2%	
	hf-PGA score ≥3	48 (23%)	23 (22%)	
	Moderate (3)	65%	83%	
	Severe (4)	35%	17%	

 44% of pts had >1 high-impact site involved

Pts With High-impac Site PsO Scalp PsO (N=252, 81%)

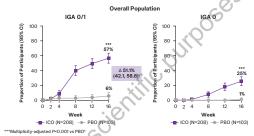
9 24

Genital PsO
(N=140, 45%) Hand/foot PsO
(N=71, 23%)

(N=71, 23%)

# ICO demonstrated significantly higher rates of IGA 0/1 vs PBO at W16 (primary endpoint)

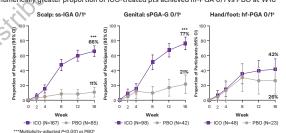
 Significantly higher proportions of ICO-treated pts reported meaningful improvement in itch (CMI PSSD Itch.<sup>ab</sup> 60% vs 14%; P<0.001) and symptom resolution at W16 (PSSD Symptom 0, ab 16% vs 3%; P<0.01)</li>



Among pts with a baseline PSSD lith score of a PSSD Symptom scole » O. I" values were based on Cocham-Marchi-Honsard oli-square est strategic by high-impact site involvement and BSA category, if approached "Internate of Higherone and BSA category, if approached "Internate and BSA category, if approached "Internate and BSA category, if approached "Internate and BSA category, if a special plant of Honorard Windows and BSA category are and "Internate America" weights. BSA-body surface area ("Recipifence internat ICO-icotokina" (ISA-investigator's Global Assessment, PBO-placeba, PSSD-Psariasis Symptom and internate and the special plant of the Assessment ("Recipifence internate and "Recipifence internate").

# ICO demonstrated significantly higher rates of clear/almost clear scalp and

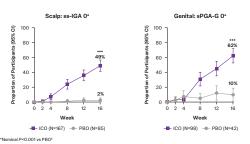
A numerically greater proportion of ICO-treated pts achieved hf-PGA 0/1 vs PBO at W16



pts with a baseline ss-IGA score, sPGA-G score, or hf-PGA score x3.1P values were based on Cochran-Mantel-Haenszel chi-square test stratified by geographic region and/or BSA ry. BSA+ody surface area, CPcconfidence interval hf-PGA-Physician's Global Assessment of hands and feet, ICO+icotrokinra, ss-IGA+Scolp-specific Investigator's Global Assessment

# ICO demonstrated higher rates of completely clear scalp and genital $\mbox{PSO}$ vs $\mbox{PBO}$

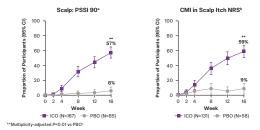
 A numerically greater proportion of ICO-treated pts achieved hf-PGA 0° vs PBO at W16 (25% vs 13%)



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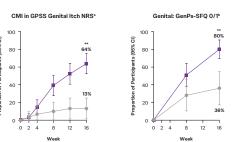
# ICO demonstrated significantly higher rates of scalp clearance and meaningful improvement in scalp itch vs PBO $\,$

ICO demonstrated early separation from PBO



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# ICO significantly improved pt-reported genital PsO itch and impact of PsO on sexual activity vs PBO



\*\*Multiplicity-adjusted P<0.01 vs P

ng pts with a baseline GPSS Genital Itah MRS soore (Item 1) 24 and as PGA-6 score 23. Minough pts with a baseline GenP-SFQ score (Item 2) 22 and as PGA-6 score 23. Product based on Cocham-MantH-Homast of Insignar test startified pts 1958 category, BRA-400 yurforce are, Cyrconfedence intervol, CMP-clinically meaningful improvement (1-p-dust) weement from baseline), GenP-SFQ-Genital Posoriasi Sexual Frequency Questionnaire, GPSS-Genital Psoriasi Symptoms Score, (ICO-icotrokinra, NRS-Numeric Rating Scote, replaceba, Pstrapticingonst, SPGA-6-Stote (Physicianis Global Assessment of Genital Psoriasis Symptoms Score, (ICO-icotrokinra, NRS-Numeric Rating Scote, replaceba, Pstrapticingonst, SPGA-6-Stote (Physicianis Global Assessment of Genital Psoriasis Symptoms Score, (ICO-icotrokinra, NRS-Numeric Rating Scote, replaceba, Pstrapticingonst, SPGA-6-Stote (Physicianis Global Assessment of Genital Psoriasis Symptoms Score, (ICO-icotrokinra, NRS-Numeric Rating Scote, Pstrapticing Sco

## Adverse event rates were generally similar between groups through W16

	ICO 200 mg QD (N=208)	PBO (N=103)
Safety through W16		
Mean weeks of follow-up	16.0	15.7
Any AE	104 (50%)	43 (42%)
Most common AEs (≥5%)		
Nasopharyngitis	26 (12%)	11 (11%)
Upper respiratory tract infection	9 (4%)	5 (5%)
Headache	6 (3%)	6 (6%)
SAE <sup>a</sup>	1 (<1%)	2 (2%)
Infection	59 (28%)	22 (21%)
Serious infection	0	1 (1%)
AE leading to discontinuation <sup>b</sup>	4 (2%)	3 (3%)
Gastrointestinal AEs	15 (7%)	8 (8%)
Active TB	0	0
Malignancy <sup>o</sup>	1 (<1%)	0

SAEs through W16 included COVID-19 pneumonia, sepsia, sciencia, and acute respiratory failure in the PBO group; and hepatitis in the ICO group. AEs leading to discontinuation through W16 included COVID-19 pneumonia, pseriatic arthropathy, and psoriatis in the PBO group; and vision blurred, visual field defect, laryngitis fungal, malignant melanoma in aitu, and headach in the ICO group. Also in the ICO group of the ICO group of the ICO group of the ICO group. The ICO group is the ICO group of the ICO group of the ICO group. The ICO group of the ICO group of the ICO group of the ICO group of the ICO group.

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