



COMPANY OVERVIEW

Dinesh V. Patel, Ph.D.
President & CEO

May 15, 2025

Forward-looking Statements

This presentation and the accompanying oral presentation contain forward-looking statements made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. All statements other than statements of historical facts contained in this presentation, including statements regarding our future results of operations and financial position, business strategy, product candidates, capital resources, potential markets for our product candidates, our plans and expectations related to the impact on our business or product candidates of actions or determinations of the U.S. Food and Drug Administration (“FDA”), our collaboration with Johnson & Johnson Innovation, Inc. (“JNJ”), our collaboration with Takeda, our IL-17 and other discovery and pre-clinical programs including expectations regarding announcements related to those programs, our potential receipt of milestone payments and royalties under our collaboration agreements with JNJ and Takeda, and the timing of icotrokinra (JNJ-2113, formerly PN-235) and rusfertide clinical results, Janssen’s development plan for icotrokinra, and the potential market opportunity for rusfertide and icotrokinra, are forward-looking statements. In some cases, you can identify forward-looking statements by terminology such as “anticipate,” “believe,” “continue,” “could,” “estimate,” “expect,” “intend,” “may,” “plan,” “potentially,” “predict,” “should,” “will,” or the negative of these terms or other similar expressions.

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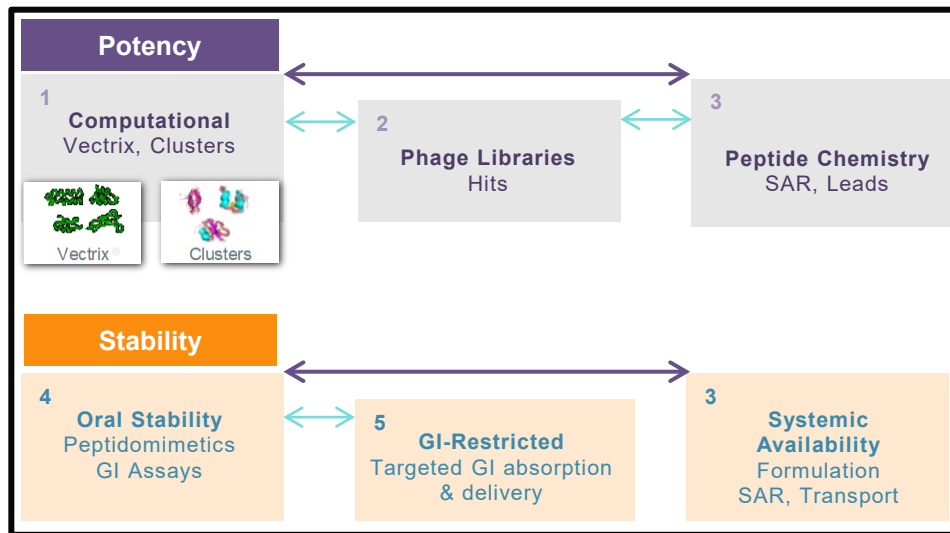
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A Peptide Therapeutics Company

Two Late-Stage Assets with Potential for NDA Filings in 2025

- Biologically and commercially validated targets
 - Immunology & inflammation, hematology, and metabolic diseases
- Protagonist peptides offer strong differentiation vs existing therapies

Peptide Technology Platform



Products

Oral Peptide
Agonist
Anti-Obesity

Oral Hepcidin
Program
Hematology

PN-881
Oral
IL-17 Antagonist
DC**

Icotrokinra
Oral IL-23r Antagonist
Psoriasis*, Ph3
Johnson & Johnson
Innovative Medicine

Rusfertide
SC Weekly Hepcidin
Mimetic
PV, Ph3
Takeda

Discovery → DC IND-Enabling → Ph 1**

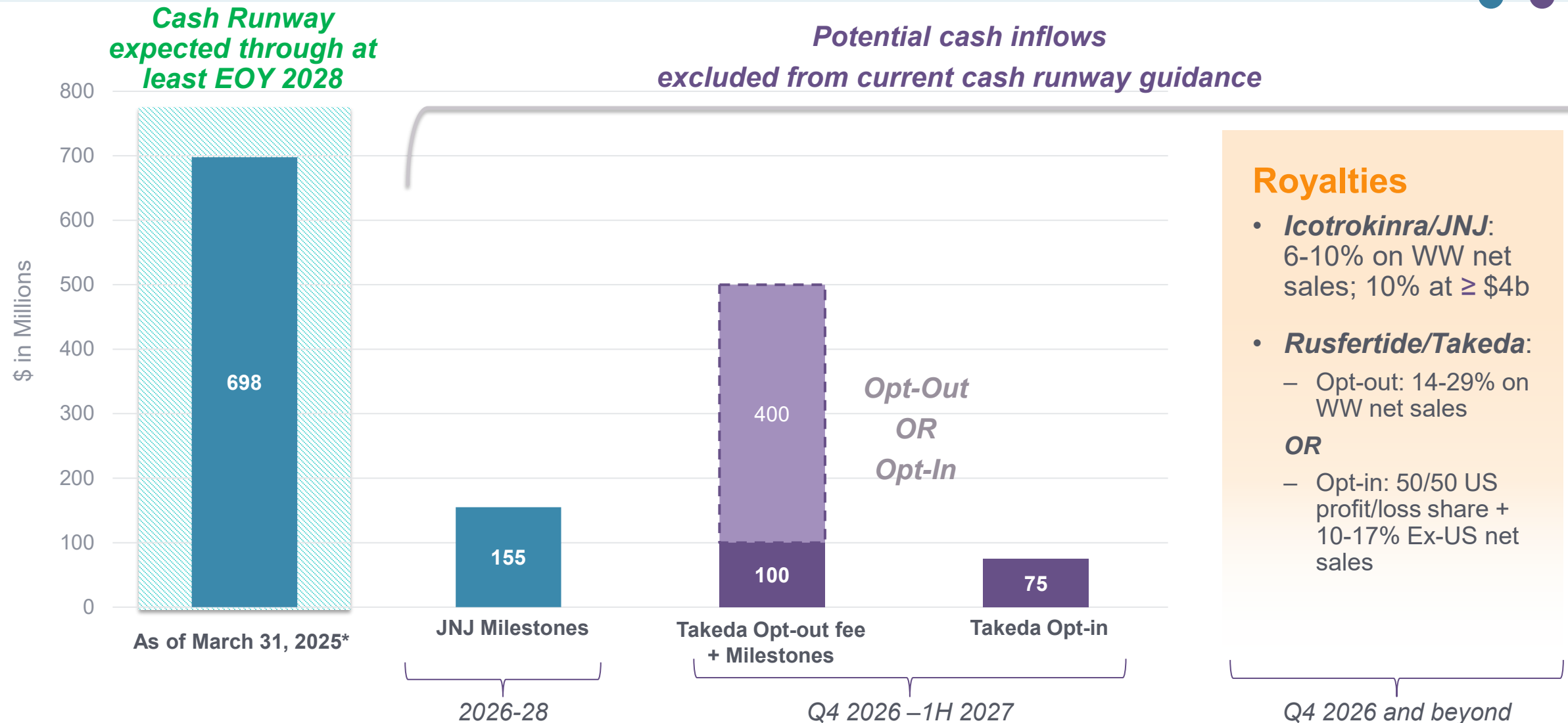
Ph 3 → NDA

Pipeline of Proprietary and Partnered Programs

Programs & Assets		Discovery/Preclinical → IND-enabling	Phase 1	Phase 2	Phase 3	NDA filing	Key Milestones
INFLAMMATION & IMMUNOLOGY	Icotrokinra Oral IL-23R Peptide Antagonist Johnson & Johnson Innovative Medicine	Moderate-to-Severe Psoriasis FRONTIER-1 & 2 Ph2b, ICONIC-LEAD Ph3, ICONIC-TOTAL Ph3, ICONIC-ADVANCE-1&2 Ph3, ICONIC-ASCEND Ph3 study planned					• NDA filing '25
		Psoriatic Arthritis ICONIC PsA-1 & -2 Ph3 initiated					
		Ulcerative Colitis ANTHEM-UC Ph2b completed; new clinical studies planned					
		Crohn's Disease Clinical study planned					
	PN-881 Oral IL-17 Antagonist	Psoriasis, Psoriatic Arthritis, Hidradenitis Suppurativa, Spondyloarthritis IND-Enabling Studies					• Phase 1 initiation Q4 '25
HEMATOLOGY	Rusfertide SC Hepcidin Mimetic Takeda	Polycythemia Vera REVIVE Ph2, THRIVE Ph2, PACIFIC Ph2 VERIFY Ph3					• NDA filing Q4 '25 • ASCO '25 plenary session
	Oral Hepcidin	Polycythemia Vera, Hereditary Hemochromatosis, Other Pre-clinical					• Development candidate Q4 '25
METABOLIC	Oral Anti-Obesity Program	Obesity & associated Co-morbidities Peptide A: Pre-clinical Peptide B: Pre-clinical Peptide C: Pre-clinical					• Development candidate(s) '25

Protagonist On a Transformative Path Leading to Significant Potential Cash Inflows

2025-2028



Capital Allocation Considerations

- Internal R&D investments
 - Develop internal programs up to clinical value inflection point
 - Oral IL-17 antagonist PN-881
 - Oral hepcidin mimetic/ferroportin blocker
 - Oral anti-obesity peptide(s)
 - New targets where peptides offer a strong differentiation
- Inorganic growth
 - Opportunistic in-licensing/acquisition of technologies, programs, assets
- Capital distribution
 - Meaningful return of capital to shareholders at the right time
 - Share buy back program

Icotrokinra (JNJ-2113)

JNJ and Protagonist Collaboration

\$337.5M

*Upfront + milestones achieved
to-date*

\$630M

*future potential development and sales
milestones*

6% to 10%

Royalty

10% at ≥ \$4B net sales

Potential milestones through 2028

Expected

Any indication	Receipt of marketing approval	\$50M	~2026
2 nd indication	NDA filing acceptance	\$25M	~2027
	Receipt of marketing approval	\$45M	~2028
3 rd indication	NDA filing acceptance	\$35M	~2028
	Total upcoming potential milestones	\$155M*	

Rusfertide Co-Development and Co-Commercialization Partnership with Takeda

Takeda Partnership overview

- January 2024; \$300M upfront received
- **Co-development**
 - Protagonist: Phase 3 completion and NDA filing
 - Takeda: Pre-commercial activities
- **Co-commercialization**
 - USA: 50:50 profit/loss share; commercial infrastructure not required for Protagonist
 - Ex-US: Takeda
- **Economics - Optionality**

Scenario	Total \$\$ upfront + milestones	Upfront	Payable Opt-Out	Potential Milestones	Royalty Rates	Comment
OPT-IN	\$630M	\$300M ✓	-	\$330M	10-17% Ex-US	50:50 US profit/loss share
OPT-OUT	\$1,675M	\$300M ✓	\$400M	\$975M	14-29% worldwide	Exclusive US rights to Takeda

Potential 2025-26 Milestones

- **\$25M ✓**
Phase 3 VERIFY study 1° endpoint achievement
- **\$50M (opt-in) or \$75M (opt-out)**
NDA approval

Financial Highlights

Financial Resources Forecast Extends Through At Least Q4 2028

CASH,
CASH EQUIVALENTS &
MARKETABLE SECURITIES

\$697.8M

as of
March 31, 2025

CASH RUNWAY
FORECAST THROUGH
AT LEAST

Q4 2028*

*Based on cash, cash equivalents and marketable securities as of March 31, 2025, but excluding additional milestone payments, potential opt-out payments and future royalties

SHARES
OUTSTANDING

~61.9M

as of
March 31, 2025



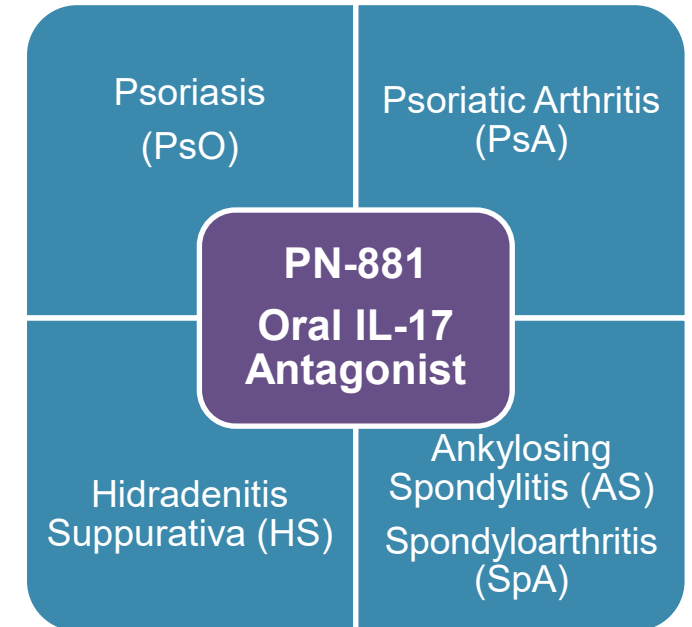
**PN-881:
Oral Peptide IL-17
Antagonist Development
Candidate**



PN-881: Oral IL-17 Peptide Antagonist Program

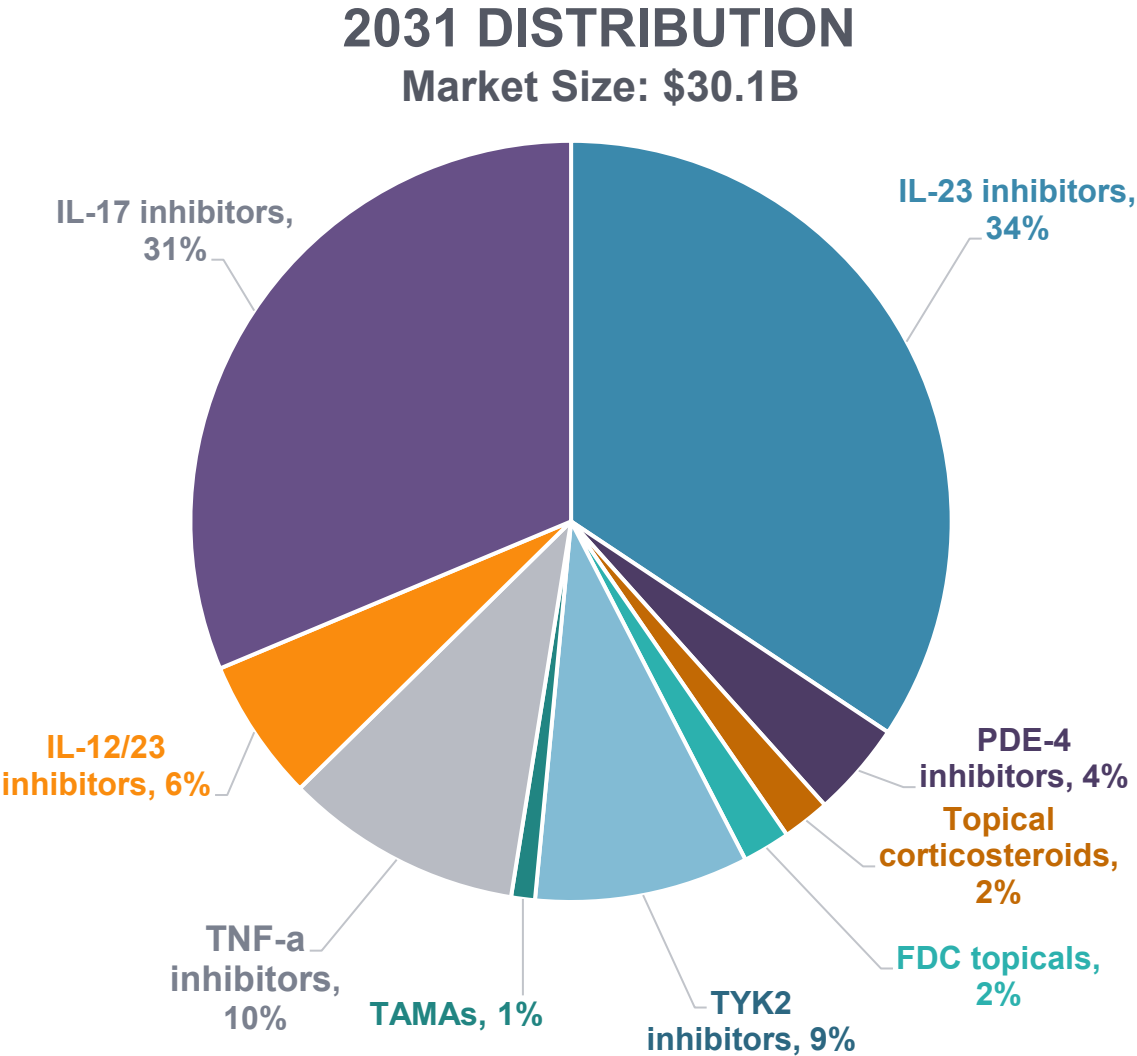
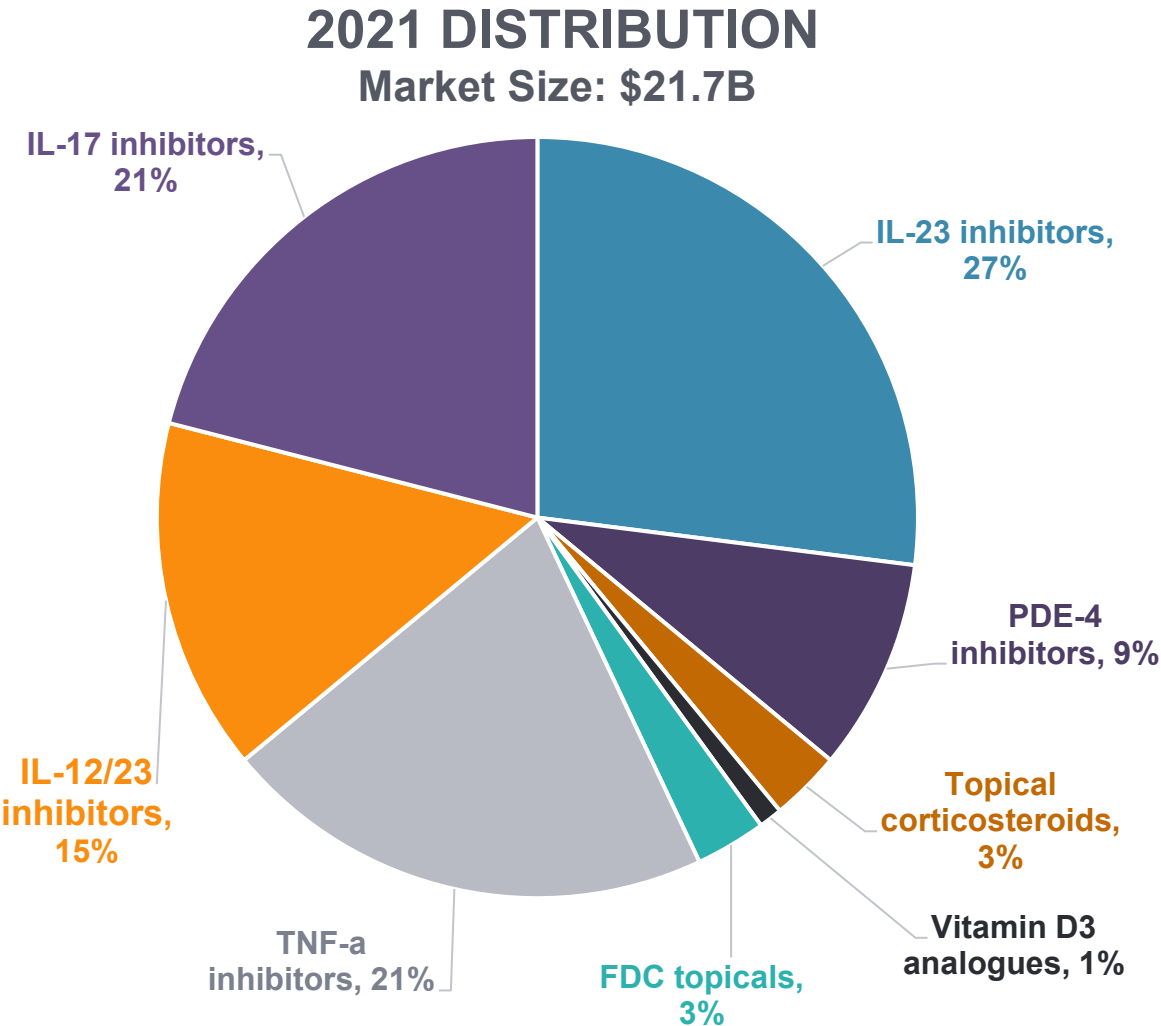
Best-in-Class Oral IL-17 Antagonist Potential

- IL-17: Clinically & commercially validated target¹:
 - Cosentyx®, Taltz®, Bimzelx®
 - Expected to capture 31% of the PsO market by 2031, generating \$9.3B
 - Growth from PsA, HS, and AS/SpA → additional sales of \$7.7B by 2034
- **PN-881**: Differentiated target product profile (TPP)
 - **Potential for best-in-class oral peptide IL-17 antagonist²**
 - Specificity for IL-17A and IL-17F ligands (IL-17 AA, AF & FF)³
- Next Steps
 - Phase 1 SAD/MAD⁴ study initiation ~Q4 2025
 - Phase 1 results → phase 2 psoriasis study
 - Rapid expansion into other IL-17-mediated diseases

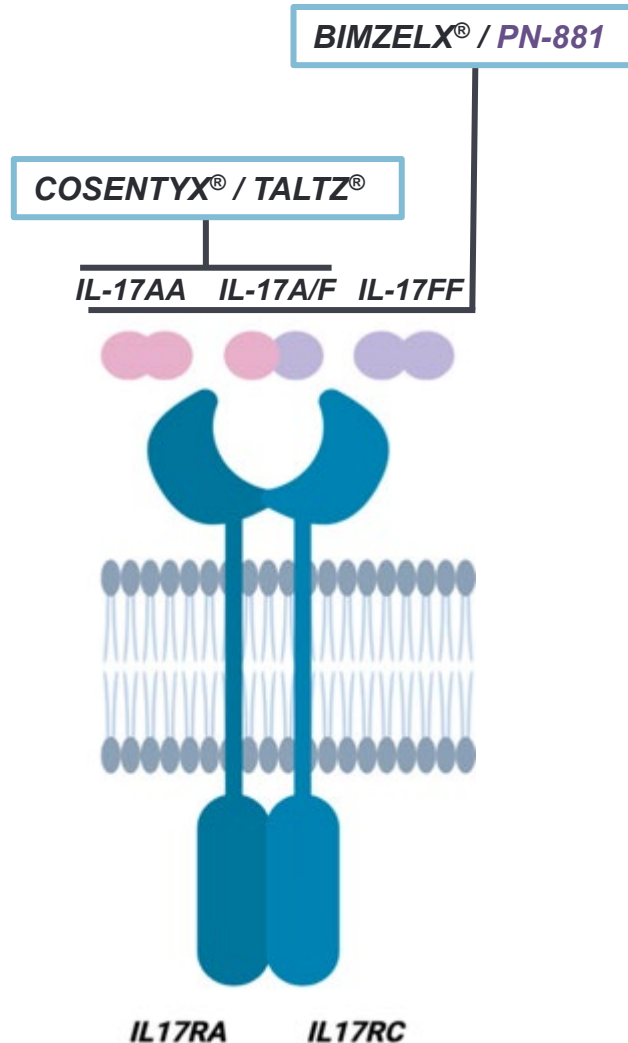


Psoriasis Market Share by Drug Class

IL-17 and IL-23 Inhibitors Expected to Dominate Market Share

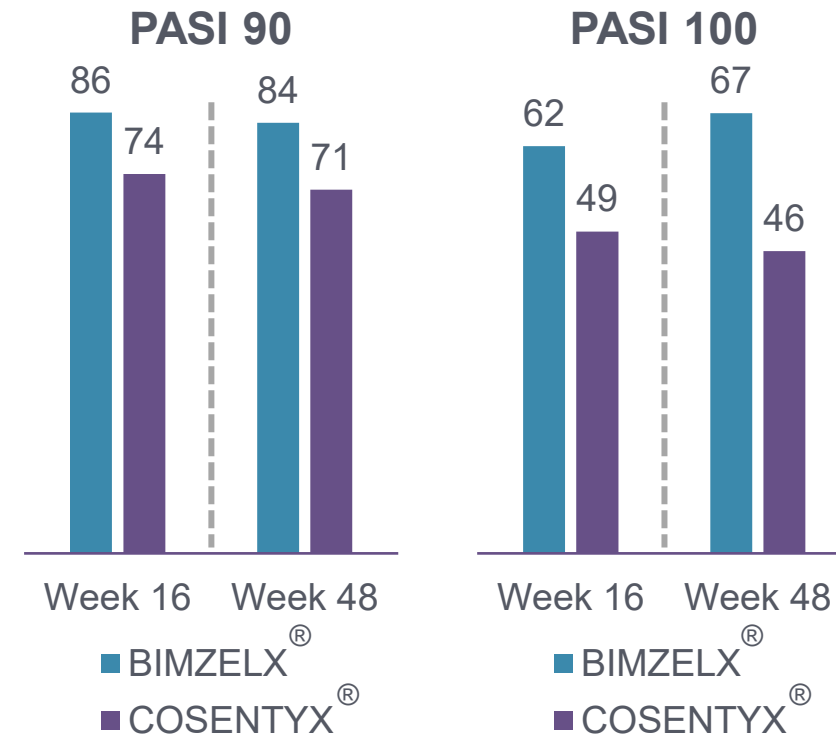


IL-17 Receptor Activated by Three Dimeric Forms of IL-17: IL-17AA, AF, and FF¹



BE RADIANT Clinical Trial:

Blockade of IL-17A and F Yields Greater Efficacy in Psoriasis¹



Selection of IL-17 Antagonist PN-881 as Development Candidate

Attribute	Criteria
Potency	• Sub-nM potency vs IL-17 AA ✓ • Blocks three dimeric forms of IL-17: AA, AF, FF ✓
Stability	• Stable in simulated gastric and intestinal fluids ✓ • Stable in serum with $t_{1/2} > 24$ hr ✓ • Metabolic stability ✓ • Thermostability ✓
<i>In vivo</i> Pharmacokinetics	• Mouse ✓ • Rat ✓ • Dog ✓ • Cynomolgus monkeys ✓
<i>In vivo</i> Pharmacodynamics	• Reduction in IL-17-induced CXCL1 after oral administration ✓
Tissue Distribution	• Mouse ✓ • Mini-pig ✓
Efficacy Model	• Rat IL-23-induced skin inflammation model ✓

PN-881 Potently Inhibits IL-17A and IL-17F

Similar potency as Bimzelx and ~100-fold more potent than Cosentyx

PN-881 vs Competitors	HT-1080 (nM) ¹					
	IL-17AA		IL-17AF		IL-17FF	
	IC ₅₀	IC ₉₀	IC ₅₀	IC ₉₀	IC ₅₀	IC ₉₀
Oral agents						
PN-881	0.13	0.56	27	55	14	76
DC-806 ² (or close analogue)	228	3323	ND	ND	Inactive	Inactive
Injectable agents						
Cosentyx [®]	11	118	151	604	Inactive	Inactive
Taltz [®]	0.12	0.35	ND ³	ND ³	Inactive	Inactive
Bimzelx [®]	0.17	0.32	19	26	13	16

1. Similar results observed in human dermal neonatal fibroblasts (HDFn) after stimulation with IL-17AA, IL-17AF, or IL-17FF

2. Compound #166 from DICE patent: US 2020/0247785 A1. DC-806 development discontinued & replaced with DC-111

3. ND = Not determined



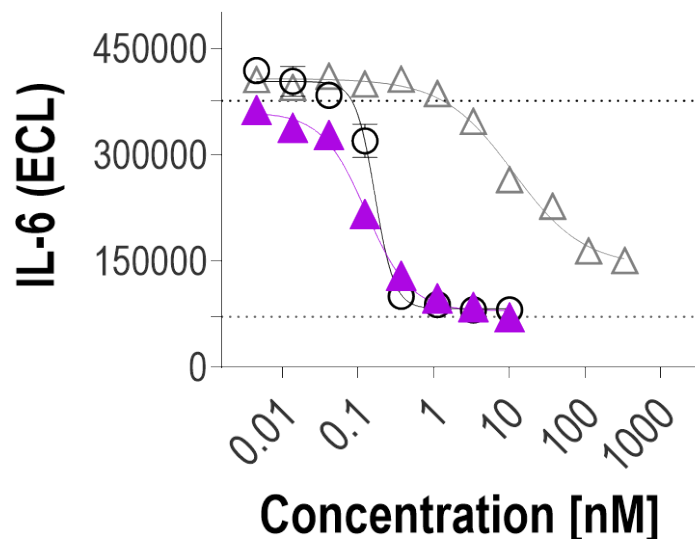
**PN-881:
Nonclinical Data Presented at
2025 Society For Investigative
Dermatology (SID) Meeting**

7-10 May; San Diego, California

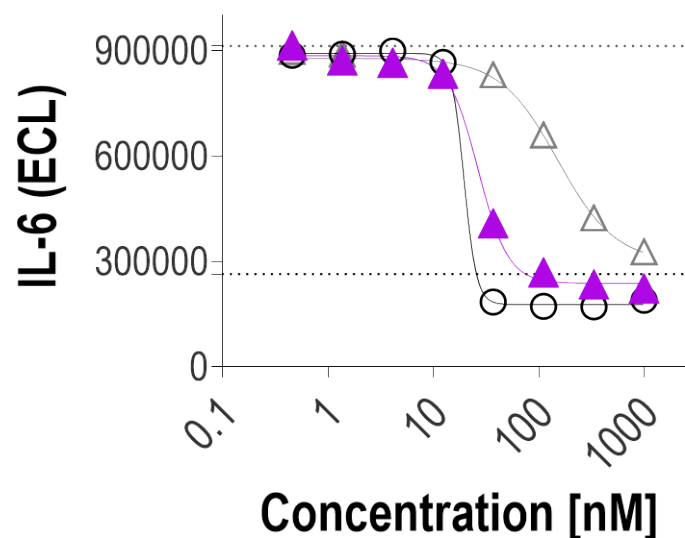


PN-881 Potently Inhibits IL-17-Induced Responses in HT-1080 Cell Line

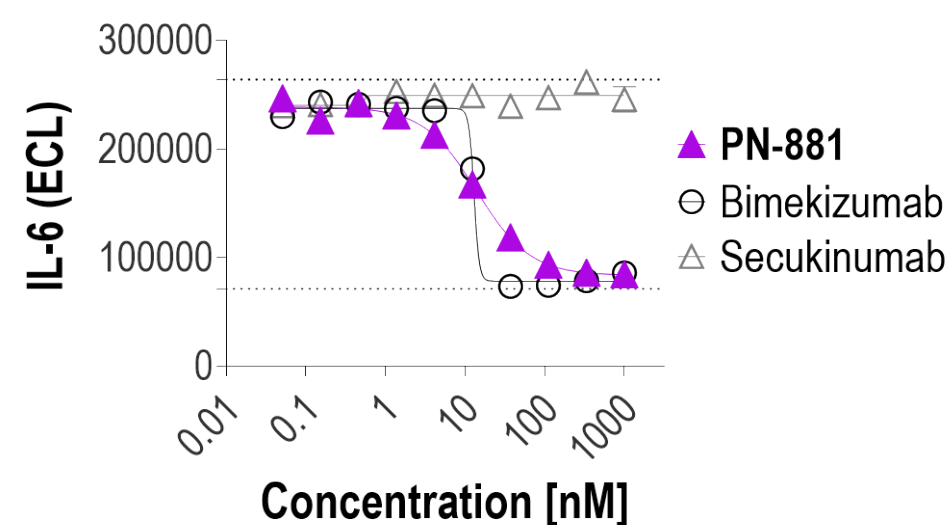
hIL-17AA



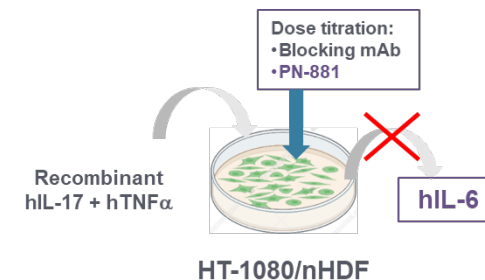
hIL-17AF



hIL-17FF



- **PN-881** has similar blocking curves as **bimekizumab** while **secukinumab's** curves for IL-17AA and IL-17AF are shifted to the right
- **Secukinumab** does not block IL-17FF



PN-881 Potently Inhibits IL-17AA and IL-17FF

Similar Potency as Bimekizumab and ~70-fold More Potent than Secukinumab

HT-1080 IC ₅₀ (nM)				
		IL-17 AA	IL-17 AF	IL-17 FF
PN-881	oral	0.13	27	14

nHDF IC ₅₀ (nM)		
IL-17 AA	IL-17 AF	IL-17 FF
0.15	29	15

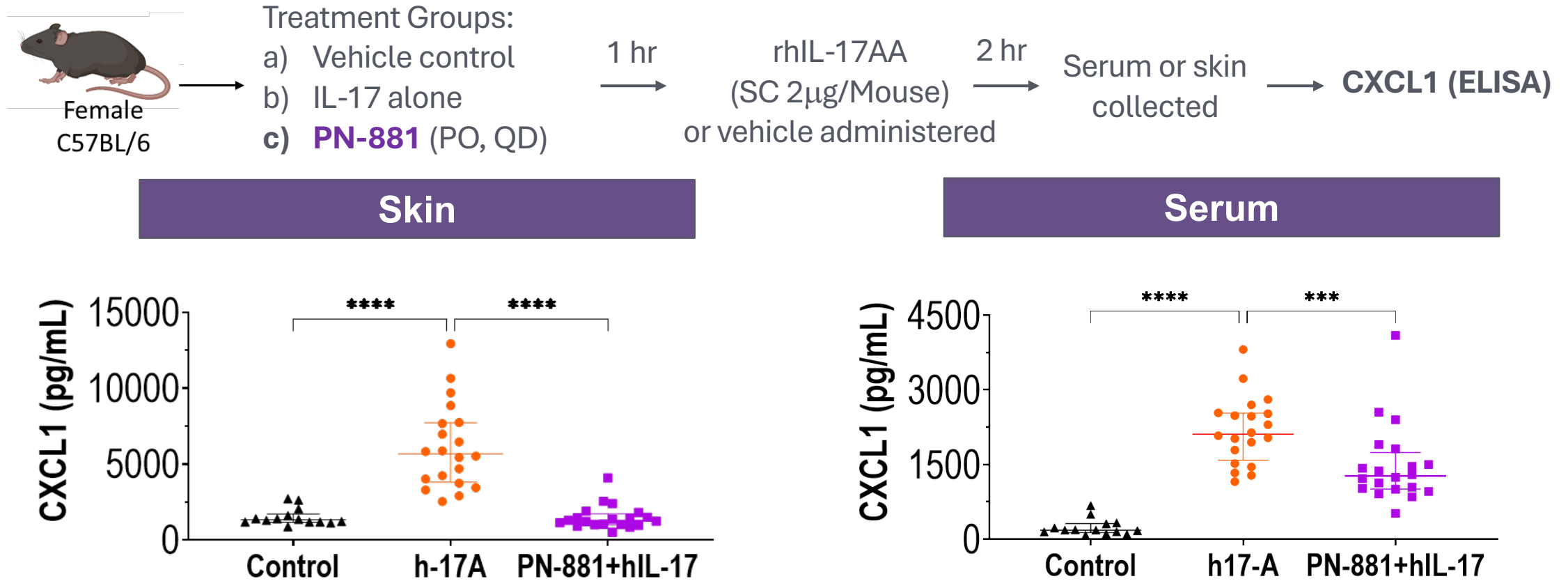
		IL-17 AA	IL-17 AF	IL-17 FF
Bimekizumab	SC	0.17	19.5	13
Secukinumab	SC	11	151	Inactive

IL-17 AA	IL-17 AF	IL-17 FF
0.12	18	14
10	175	Inactive

- **PN-881** has sub-nM IL-17AA blocking potency (IC₅₀) similar to **bimekizumab** and 70 times more potent than **secukinumab**
- **PN-881** inhibited IL-17 AF and FF with similar potency than **bimekizumab**

Oral PN-881 Neutralizes Human IL-17 in Mouse IL-17 Challenge PD Model

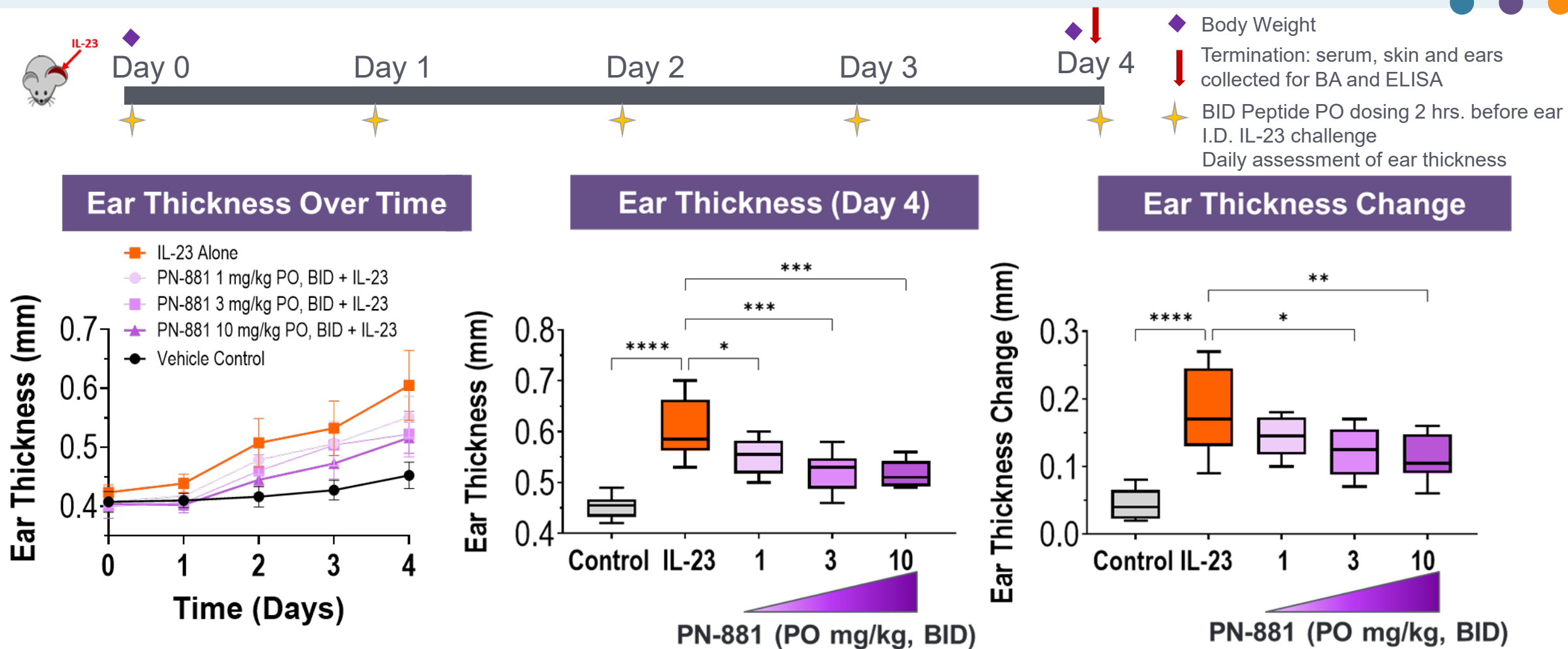
PN-881 Significantly Reduces Serum and Skin CXCL1 Levels After Oral Administration



- Human IL-17 s.c. challenge induced systemic and skin production of CXCL1
- Oral administration of **PN-881** significantly reduced CXCL1 responses in serum and skin

Oral PN-881 in the Rat IL-23-Induced Skin Inflammation Efficacy Model

PN-881 Significantly Reduces IL-23-Induced Ear Thickness After Oral Administration



*p<0.05, **p<0.01, ***p<0.001, ****p<0.0001. Data points depict mean $\pm$ standard deviation, Boxes depict median and interquartile ranges; bars depict min. and max.



PN-881: Summary



PN-881 Achieves Desired Pharmacology in Preclinical Models



- High systemic exposures after oral administration to mice, rats, dogs, and cynomolgus monkeys
 - >100 ng/mL in cynomolgus monkeys with oral dose of 2.5 mg/kg
- Blockade of IL-17 in *in vivo* mouse models after oral administration
 - PN-881 inhibits CXCL1 production in serum and in skin in mice challenged with supra-physiologic doses of human IL-17
 - PN-881 shows efficacy at doses as low as 1 mg/kg BID in inhibiting ear inflammation (erythema and thickness) in rats challenged with repeated IL-23 injections
- Suitable tissue distribution into the skin in preclinical models
 - Ratio of skin to plasma concentrations comparable to or better than monoclonal antibodies

PN-881: Near-Term Clinical Development Plan



H1 2025	H2 2025	H1 2026	H2 2026
❖ IND-Enabling Studies ❖ SID'25 Meeting oral presentation: nonclinical data	❖ Initiation of 3-month Tox Studies ❖ Phase 1 Initiation	❖ Phase 1 Topline PK/PD Results	❖ Phase 2 Initiation



Johnson & Johnson
Innovative Medicine

Icotrokinra (JNJ-2113, formerly PN-235): Oral IL-23 Receptor Antagonist Peptide

Targeted Investigational Therapy for
Psoriasis & Other IL-23 Mediated Diseases



Icotrokinra: First- and Only-in-Class ORAL IL-23 Receptor Antagonist in Clinical Development

JNJ Partnership overview

- 2017 to present: Icotrokinra
 - Protagonist completed pre-clinical and first Ph1 study
 - JNJ responsible for further development and commercialization
- **Successful outcome in Phase 3 psoriasis studies**
- **Successful outcome in Phase 2b ulcerative colitis study**
- Potential peak sales: **\$5B+**^{1,2}
 - Psoriasis, psoriatic arthritis, ulcerative colitis, Crohn's disease

Approved Injectable
IL-23 Antagonist mAbs

Stelara®

Skyrizi®

Tremfya®

\$337.5M *Upfront +
milestones
achieved to-date*

\$630M
*Future
potential milestones*

**6% to 10%
Royalty**
10% at ≥ \$4B net sales

Icotrokinra Clinical Development Program

Successful Studies in Psoriasis & UC; PsA studies Ongoing; CD study planned

Plaque Psoriasis

FRONTIER 1 & 2 Ph2b, n = 255 & 227, in moderate-to-severe psoriasis



Bissonnette R. et al. *New Engl Med*; 2024;390:510-521

ICONIC-LEAD Ph3, n = 684, in moderate-to-severe psoriasis



ICONIC-TOTAL Ph3, n = 311, psoriasis in special areas of body



ICONIC-ADVANCE 1 Ph3, n = 774, Icotrokinra vs. Deucravacitinib



ICONIC-ADVANCE 2 Ph3, n = 731, Icotrokinra vs. Deucravacitinib



Pustular/Erythrodermic Psoriasis Ph3, n = 19

• On-going

ICONIC-ASCEND Ph3, n = 675, Icotrokinra vs. Ustekinumab

• Planned

Psoriatic Arthritis

ICONIC-PsA 1 Ph3, n~540, in biologic-naive active psoriatic arthritis

• On-going

ICONIC-PsA 2 Ph3, n~750, in biologic exposed active psoriatic arthritis

• On-going

Ulcerative Colitis

ANTHEM-UC Ph2b, n = 252, in ulcerative colitis



New clinical study in ulcerative colitis

• Planned

Crohn's Disease

Clinical study in CD

• Planned

**Psoriasis
NDA filing
2025**

Psoriasis

- Aiming to redefine the standard of care with icotrokinra for people living with plaque psoriasis
 - Potential first-line therapy for treatment of psoriasis
- Icotrokinra is the first targeted oral peptide that selectively blocks the IL-23R and shows potential to offer patients the combination of complete skin clearance and a favorable safety profile in a once daily pill
 - Potential to transform treatment paradigm in plaque psoriasis
 - Nearly half the patients (46%) and three fourth of adolescents (76%) achieved completely clear skin (IGA 0) at 24 weeks

Ulcerative Colitis

- Potential to transform the treatment paradigm in ulcerative colitis
 - Clinical response rates of up to 63.5% and clinical remission rates up to 30.2% at week 12 and a favorable safety profile observed in the phase 2b ANTHEM UC study
 - Clinical response and remission rates continued to improve through week 28

Icotrokinra Market Opportunity¹

Blockbuster Potential for a Safe and Effective Oral, Once Daily Medication

Psoriasis/IBD patients
eligible for advanced
therapies, and yet aren't
receiving them²

50-70%
(~5M)

Market growth is expected
to be driven by orals⁴

75% Patients on injectables
who would switch to
an oral with similar
safety & efficacy³

Combination of advanced efficacy and trusted safety in a preferred oral formulation could unlock a large market share

1. JNJ Innovative Medicines Enterprise Business Review, Dec 5th, 2023.
2. Global Quant Patient Opportunity Research – Jan 2022 (n=378)
3. Patient Oral v Inj Preference Research – Nov 2022 (n=395) – both in patients with moderate-to-severe plaque psoriasis
4. Clarivate and 2022 Epi Reports including internal assumptions
5. Evaluate Pharma WW Sales by Indication Sep 2023 extrapolated 2028-30

ICONIC-LEAD Phase 3 Study Design

Late-Breaking Oral Presentation at 2025 AAD Meeting, March 2025

Moderate-to-severe plaque PsO (N=684)

Key inclusion criteria

- ≥12 years
- Plaque PsO for ≥26 weeks
- Body surface area (BSA) ≥10%, Psoriasis Area and Severity Index (PASI) score ≥12, and Investigator's Global Assessment (IGA) score ≥3
- Candidate for phototherapy or systemic treatment for plaque PsO

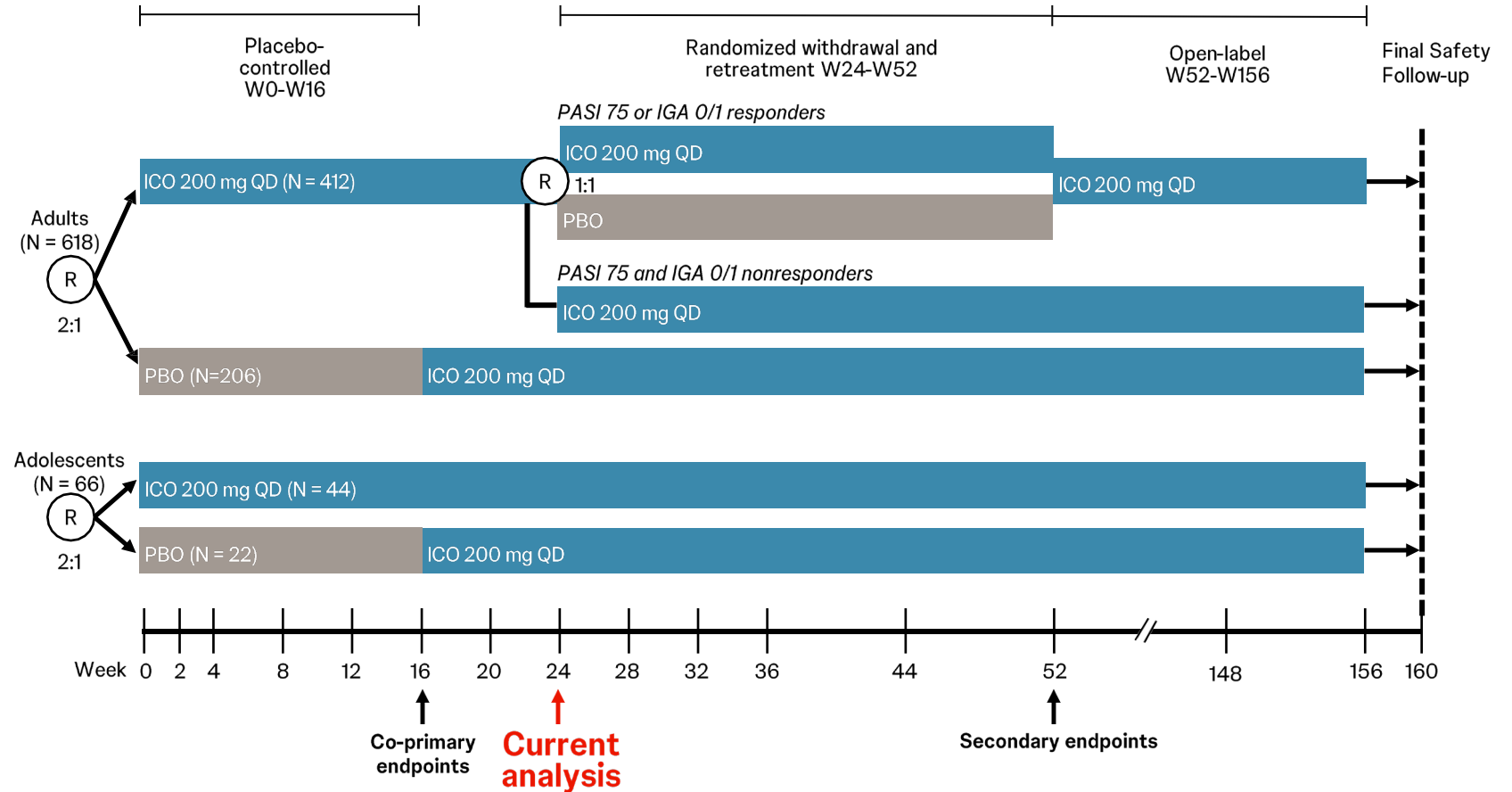
Endpoints

Co-primary endpoints:

- IGA 0/1 at W16
- PASI 90 at W16

Key secondary endpoints:

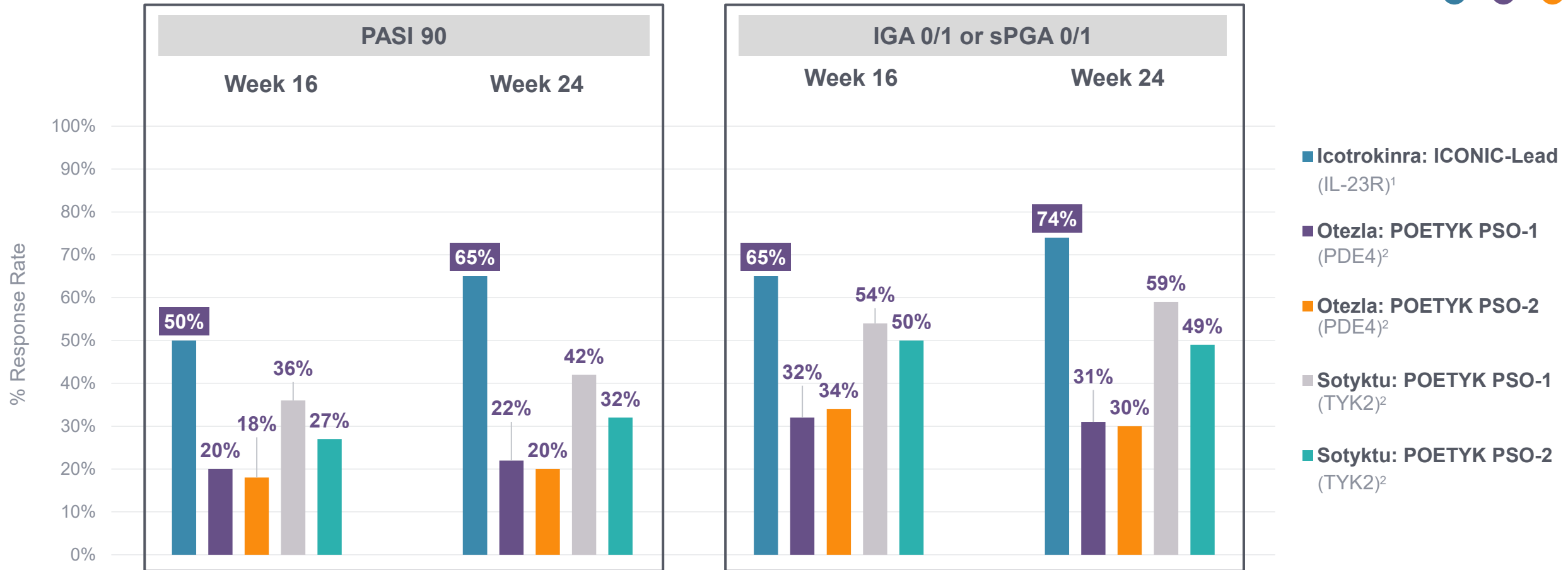
- **Clinical outcomes** (PASI 75/90/100, IGA 0) at W4, W8, and/or W16
- **PROs** (≥4-point improvement from baseline in PSSD Itch, PSSD Symptom 0) at W4, W8, and/or W16
- **Scalp PsO** (ss-IGA 0/1) at W16



Participants with the following intercurrent events were considered as nonresponders: discontinued study drug due to a lack of efficacy or AE of worsening PsO or initiated prohibited medication that could impact PsO. After accounting for these intercurrent events, nonresponder imputation was applied to participants with missing data. **AE**=adverse event, **IGA 0/1**=IGA score of 0 (clear)/1 (almost-clear) and a ≥2-grade improvement, **PASI 75/90/100**=reduction from baseline of 75%/90%/100% in the PASI score, **PBO**=placebo, **PSSD**=Psoriasis Symptom and Sign Diary, **QD**=once daily, **R**=randomization, **ss-IGA**=scalp-specific Investigator's Global Assessment, **ss-IGA 0/1**=ss-IGA score of 0 (clear)/1 (almost clear) and a ≥2-grade improvement from baseline.

Icotrokinra in ICONIC-LEAD vs Oral Approved Phase 3 Benchmarks*

Best-in-Class Oral Psoriasis Targeted Therapy Potential



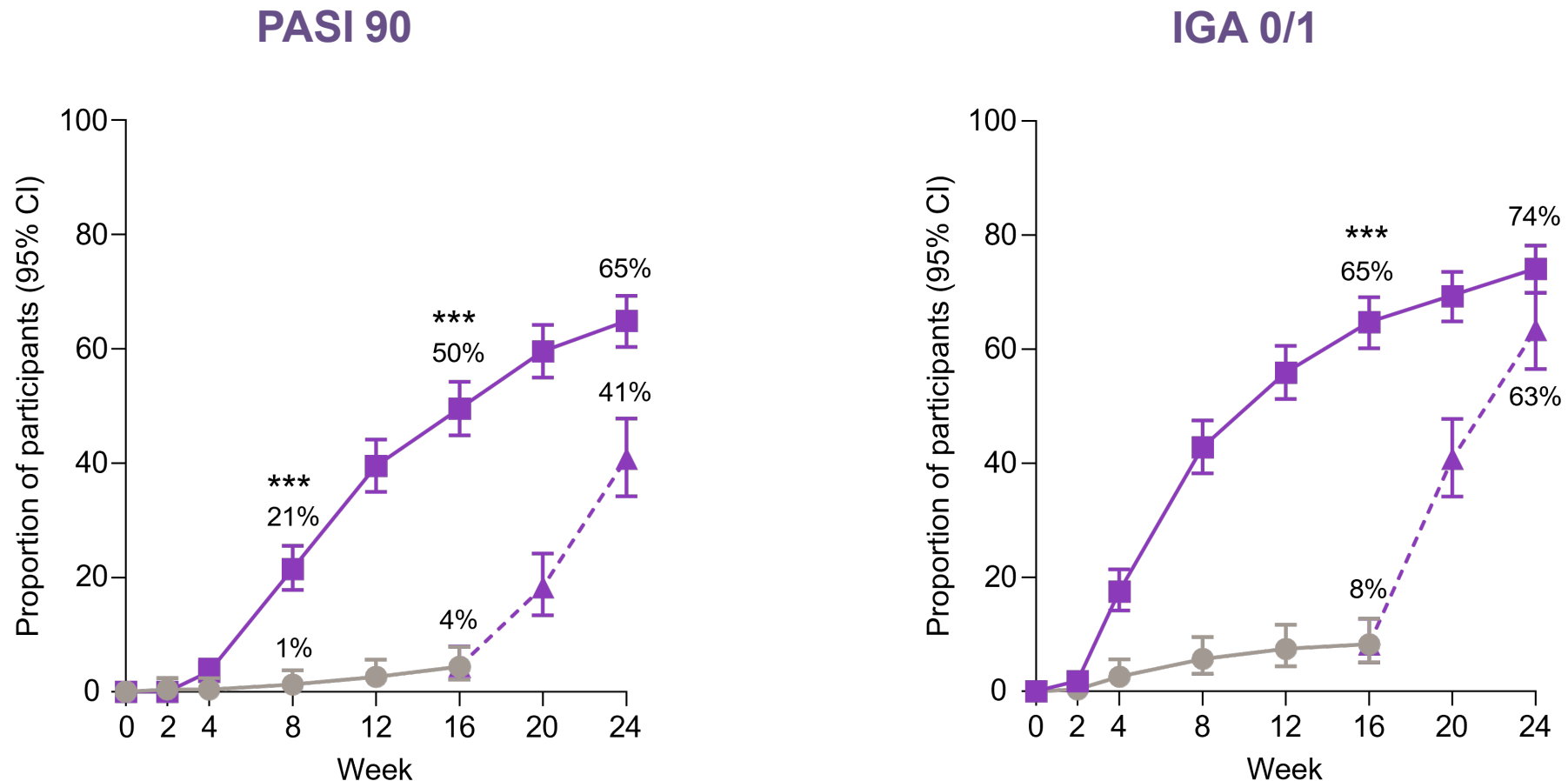
*Cross trial (not head-to-head) comparisons

1. Johnson & Johnson. "Icotrokinra delivered an industry-leading combination of significant skin clearance with demonstrated tolerability in a once daily pill in Phase 3 topline results." News release. 18 November 2024.

2. Sotyktu [package insert]. Princeton, NJ. Bristol-Myers Squibb Company. [https://packageinserts.bms.com/pi/pi_sotyktu.pdf] September 2022. Accessed on 15 November 2024.

2025 AAD Meeting: Week 24 Results

PASI 90 and IGA 0/1 Response Rates Continue to Increase Through Week 24 With Icotrokinra

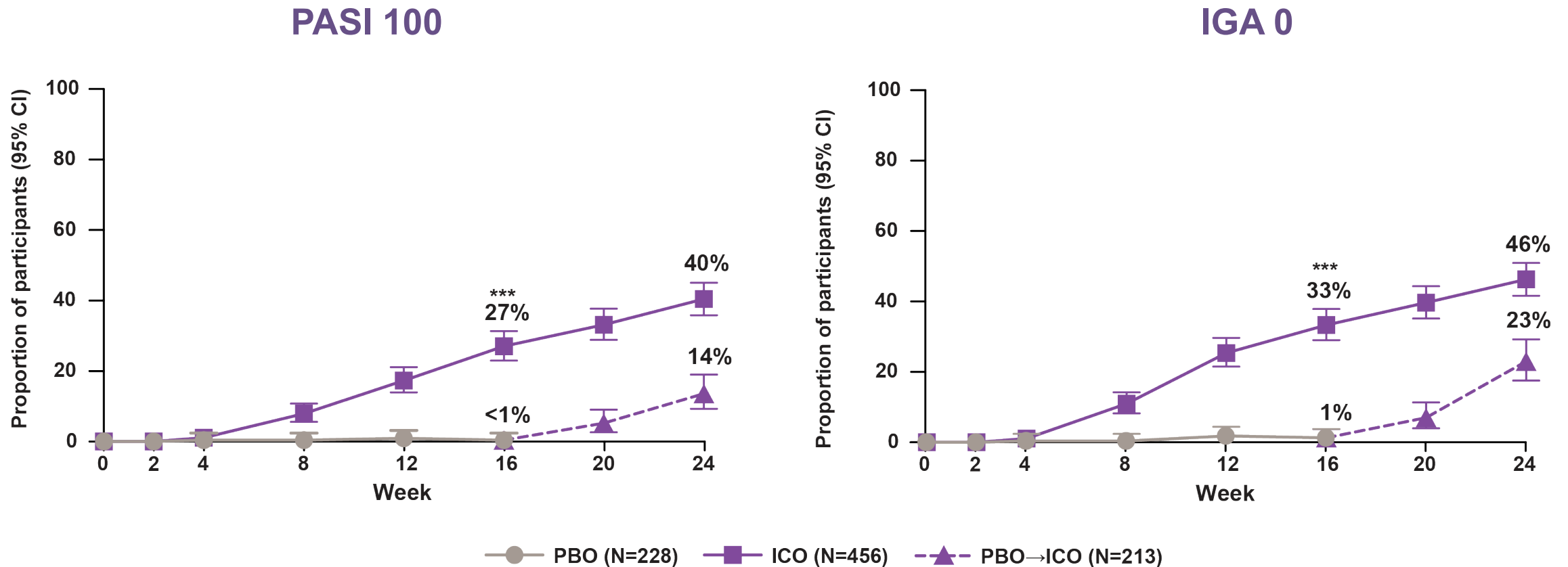


***Multiplicity-adjusted $P < 0.001$ vs. PBO^a

● PBO (N = 228) ■ ICO (N = 456) ▲ PBO → ICO (N = 213)

2025 AAD Meeting: Week 24 Results

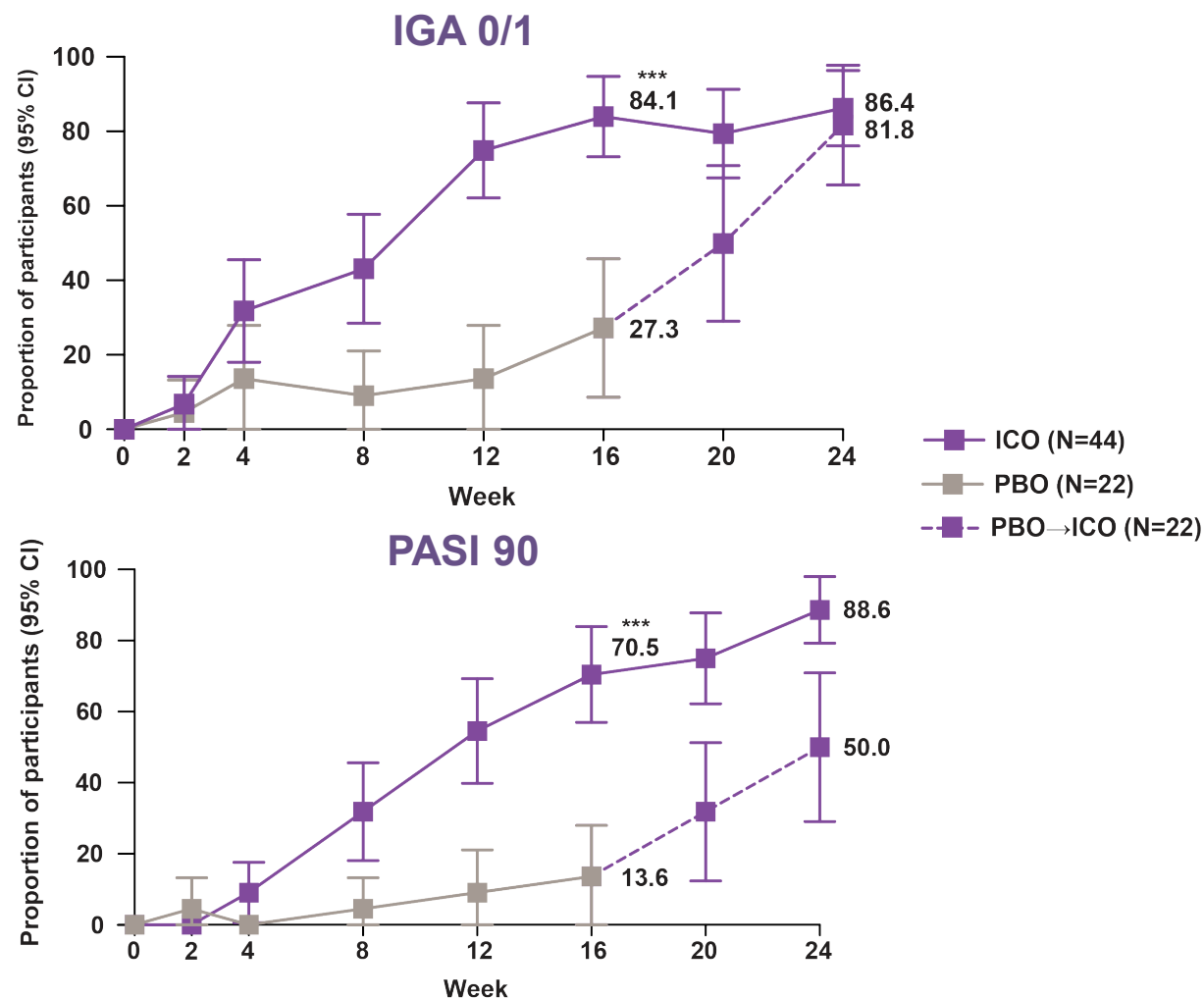
PASI 100 and IGA 0 Response Rates Continue to Increase Through Week 24 With Icotrokinra



***Multiplicity-adjusted $P < 0.001$ vs. PBO^a

2025 WCPD Meeting: ICONIC-LEAD in Adolescents

Icotrokinra Demonstrates High Response Rates in Adolescents With Moderate/Severe Plaque Psoriasis



In adolescents receiving ICO, skin response rates increased through W24:

Clear/almost clear

IGA 0/1: 86%



PASI 90: 89%



Completely clear

IGA 0: 75%



PASI 100: 64%

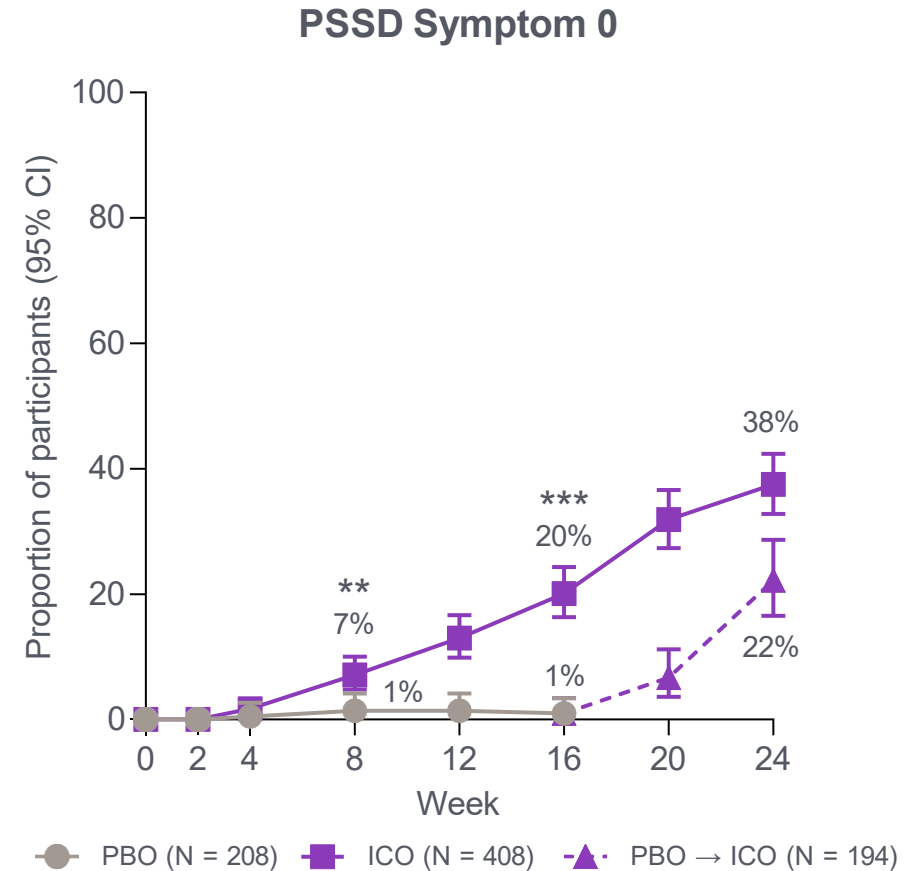
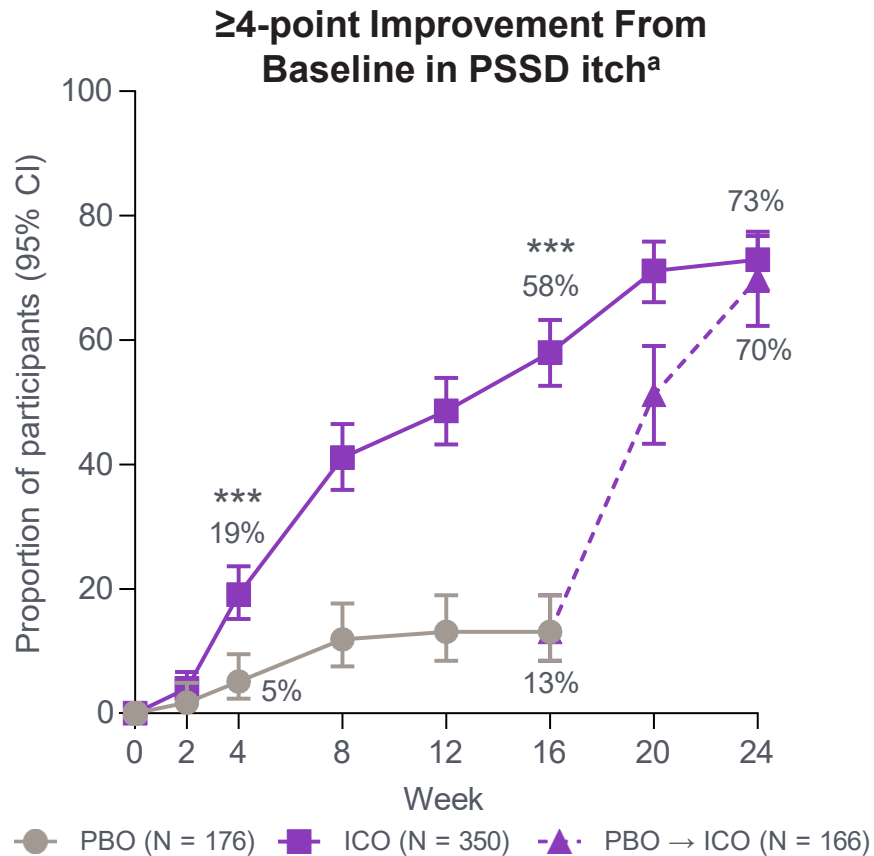


***nominal $p < 0.001$ vs. PBO; IGA 0/1 at W16: Δ 56.2% (33.2%, 74.1%); PASI 90 at W16: Δ 56.3% (32.5%, 73.0%).

Note: 95% confidence intervals (CI) are based on the normal assumption without adjustment (Wald Method). PBO→ICO includes PBO participants who crossed over to receive ICO at W16 through W24. Participants with ICE 1-2 or missing data were imputed as nonresponders through W24. P-value derived from Cochran-Mantel-Haenszel chi-square test stratified by geographic region.

2025 AAD Meeting: Week 24 Results

Significantly Higher Proportions of ICO-vs. PBO-Treated Participants Reported *Meaningful Improvements in PsO Itch*



ICO demonstrated early separation from PBO on improving itch and resolving symptoms; response rates increased through W24

2025 AAD Meeting: ICONIC-LEAD Update—Week 24 Results

AE Rates Were Generally Similar Between Groups Through Week 16

	ICO 200 mg QD (N=456)	PBO (N=228)
Safety Through Week 16		
Mean duration of follow-up, wks	15.9	15.8
Any AE	225 (49%)	112 (49%)
Most common AEs (≥5%)		
Nasopharyngitis	31 (7%)	15 (7%)
Upper respiratory tract infection	30 (7%)	16 (7%)
SAE	6 (1%)	6 (3%)
Infections	107 (23%)	51 (22%)
Serious infections	1 (<1%)	0
AE leading to discontinuation	6 (1%)	1 (<1%)
Gastrointestinal-related AE	26 (6%)	13 (6%)
Active TB	0	0
Malignancy	2 (<1%)	0

Through W24:

- Most common AEs were similar to those observed through Week 16
- No ICO safety signals emerged

ICONIC-TOTAL (NCT06095102—Plaque PsO and Difficult-to-Treat High Impact Sites)

Study Design

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

Key inclusion criteria:

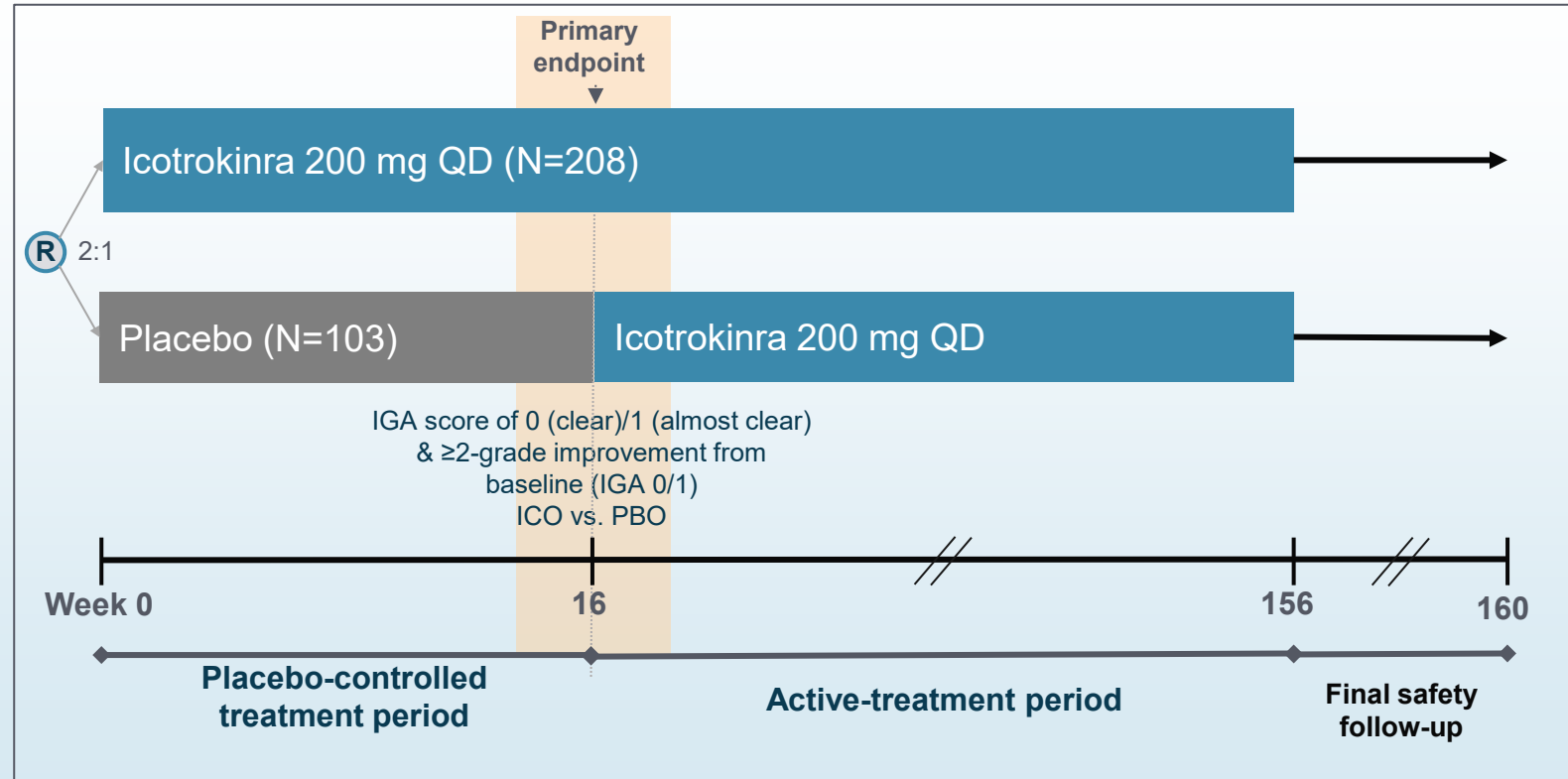
- ≥12 years old
- Plaque PsO for ≥26 weeks
- BSA ≥1% AND IGA score ≥2
- At least moderate high-impact PsO involving ≥1 site:
 - **Scalp PsO:** ss-IGA score ≥3
 - **Genital PsO:** sPGA-G score ≥3
 - **Hand/foot PsO:** hf-PGA-G score ≥3
- Candidate for phototherapy or systemic treatment for plaque PsO and failed ≥1 topical

Primary endpoint:

- ICO vs. PBO: IGA score of 0 (clear)/1 (almost clear) & ≥2-grade improvement from baseline (IGA 0/1)

Primary completion dates:

- June 2024



2025 SID Meeting: ICONIC-TOTAL—Plaque PsO and Difficult-to-Treat High Impact Sites

Baseline Characteristics Were Generally Similar Between Groups

- Overall, 5% of pts (ICO: 4%; PBO: 9%) discontinued prior to W16^d

Baseline Characteristics	ICO 200 mg QD (N=208)	PBO (N=103)
Demographics		
Age, years	45.3 (14.6)	43.5 (13.8)
Male	66%	61%
White	77%	80%
BMI, kg/m ²	29.0 (6.6) ^a	29.4 (8.1) ^a
Disease Characteristics		
PsO disease duration, years	16.8 (13.3)	15.2 (10.5)
% BSA with PsO	16.6 (13.5)	14.8 (11.7)
<10%	36%	37%
≥10%	64%	63%
IGA score		
Moderate (3)	74%	71%
Severe (4)	22%	21%
PASI (0-72)	14.6 (7.6)	14.0 (7.0)
Prior Treatment for PsO		
Phototherapy (PUVA and UVB)	43%	31%
Systemic therapy ^b	73%	73%
Biologic therapy ^c	34%	31%

Data shown are mean (SD), unless otherwise indicated.

^aICO: N=203; PBO: N=101.

^bConventional nonbiologic systemics, novel nonbiologic systemics, 1,25-vitamin D3 and analogues, phototherapy, and biologics.

^cAdalimumab, alefacept, briakinumab, brodalumab, certolizumab pegol, efalizumab, etanercept, guselkumab, infliximab, ixekizumab, natalizumab, risankizumab, secukinumab, tildrakizumab, and ustekinumab.

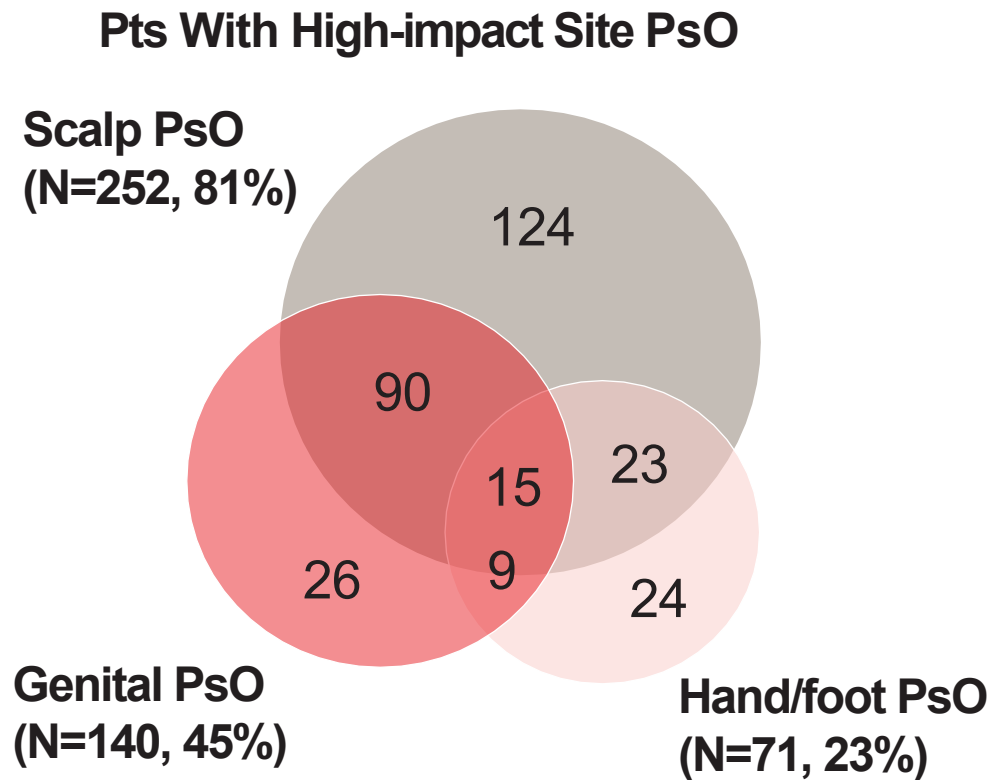
^dAmong the pts who discontinued prior to W16 (ICO: n=8 [4%]; PBO: n=9 [9%]), the most common reasons for discontinuation were lack of efficacy and AEs in the ICO group (n=3 [1%] for each) and lack of efficacy in the PBO group (n=5 [5%]).

BMI=body mass index; **PASI**=Psoriasis Area and Severity Index; **PUVA**=psoralen plus ultraviolet A; **SD**=standard deviation; **UVB**=ultraviolet B.

Scalp and Genital PsO Severity Was Generally Similar Between Groups

- Among the limited subset of pts with hf-PGA ≥ 3 , a higher proportion in the ICO group had severe involvement vs PBO
- 44% of pts had >1 high-impact site involved

High-impact Site PsO Severity ^a	ICO 200 mg QD (N=208)	PBO (N=103)
ss-IGA score ≥ 3	167 (80%)	85 (83%)
 Moderate (3)	80%	75%
Severe (4)	20%	25%
sPGA-G score ≥ 3	98 (47%)	42 (41%)
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%

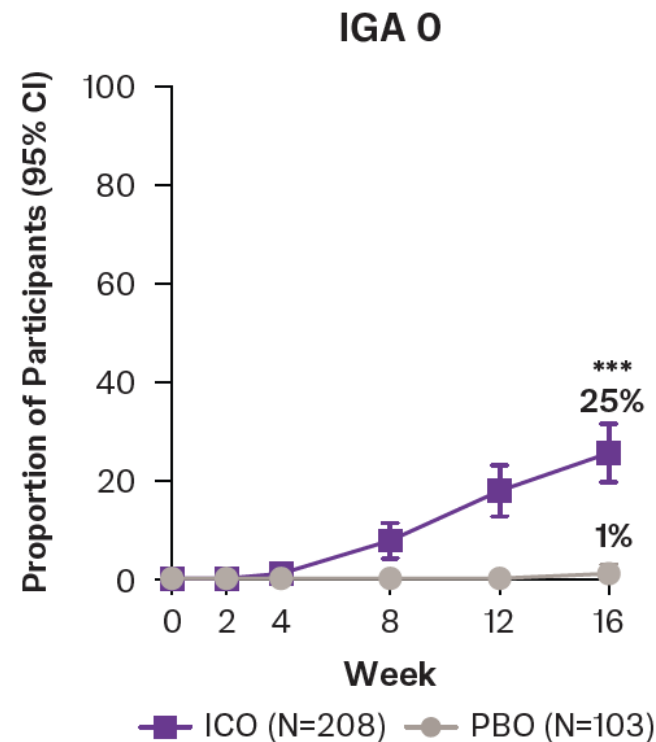
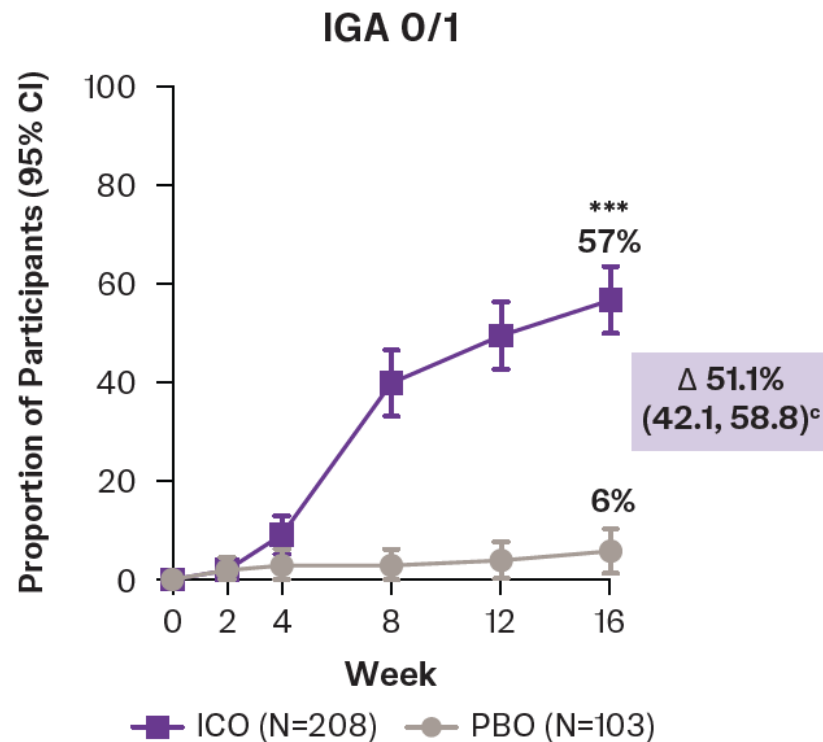


2025 SID Meeting: ICONIC-TOTAL—Plaque PsO and Difficult-to-Treat High Impact Sites

ICO Demonstrated Significantly Higher Rates of IGA 0/1 vs PBO at W16 (Primary Endpoint)

- Nearly 30% of ICO-treated pts achieved clear skin at W16
- Significantly higher proportions of ICO-treated pts reported meaningful improvement in itch (CMI PSSD Itch,^{a,b} 60% vs 14%; $P<0.001$) and symptom resolution at W16 (PSSD Symptom 0,^{a,b} 16% vs 3%; $P<0.01$)

Overall Population



***Multiplicity-adjusted $P<0.001$ vs PBO^b

^aAmong pts with a baseline PSSD Itch score ≥ 4 or PSSD Symptom score >0 .

^bP values were based on Cochran-Mantel-Haenszel chi-square test stratified by high-impact site involvement and BSA category, if applicable.

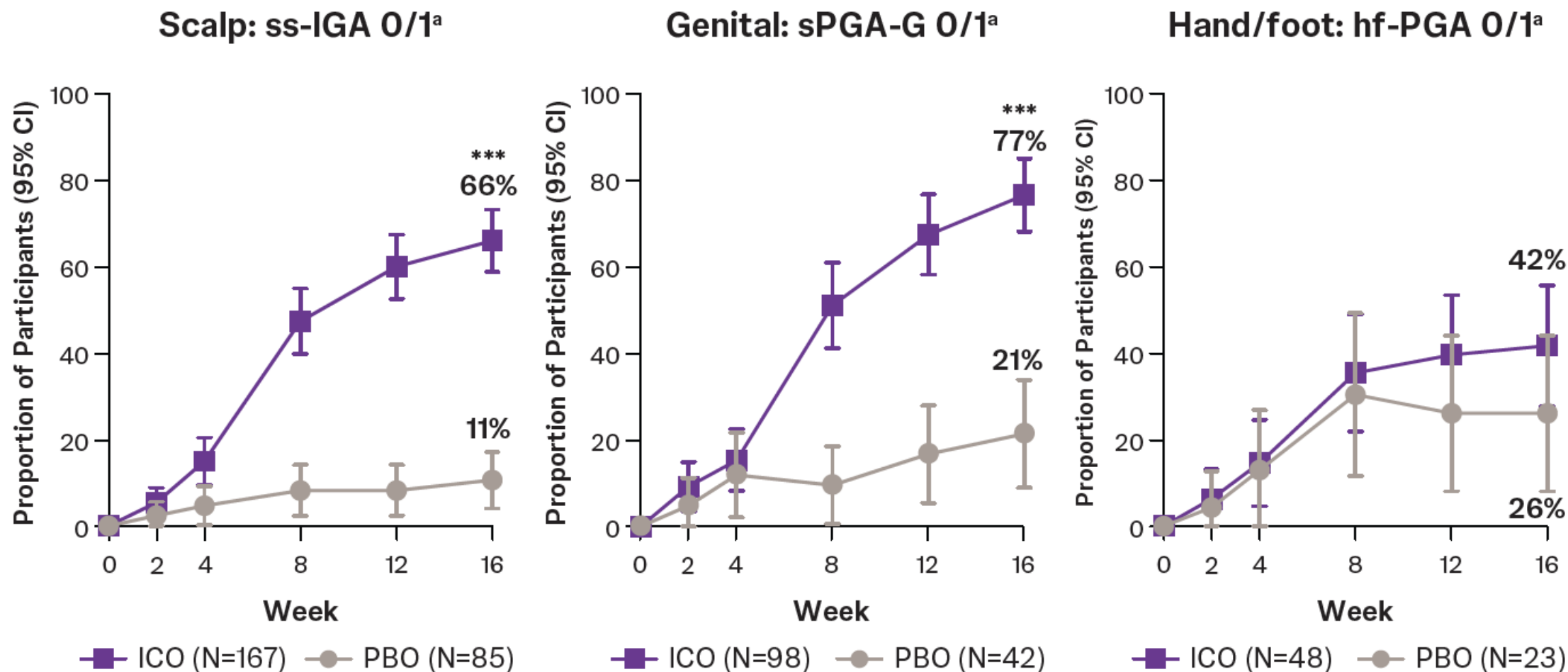
^cTreatment difference and 95% CI (using Miettinen-Nurminen method) were calculated adjusting for high-impact site involvement and BSA category using Mantel-Haenszel weights.

CI=confidence interval; CMI=clinically meaningful improvement (≥ 4 -point improvement from baseline); PSSD=Psoriasis Symptom and Sign Diary.

2025 SID Meeting: ICONIC-TOTAL—Plaque PsO and Difficult-to-Treat High Impact Sites

ICO Demonstrated Significantly Higher Rates of Clear/Almost Clear Scalp and Genital PsO vs PBO

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

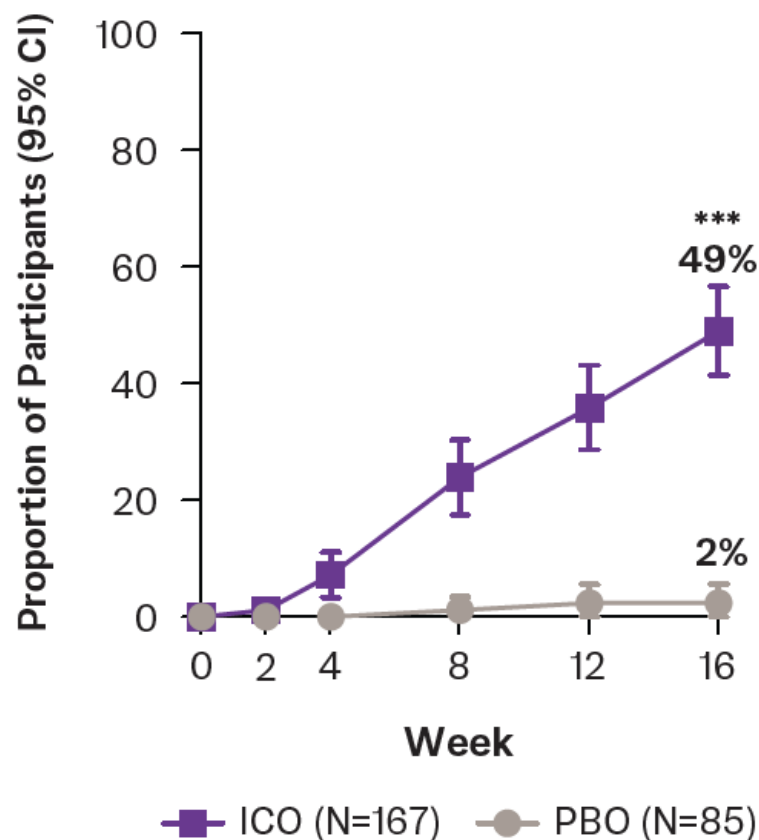


2025 SID Meeting: ICONIC-TOTAL—Plaque PsO and Difficult-to-Treat High Impact Sites

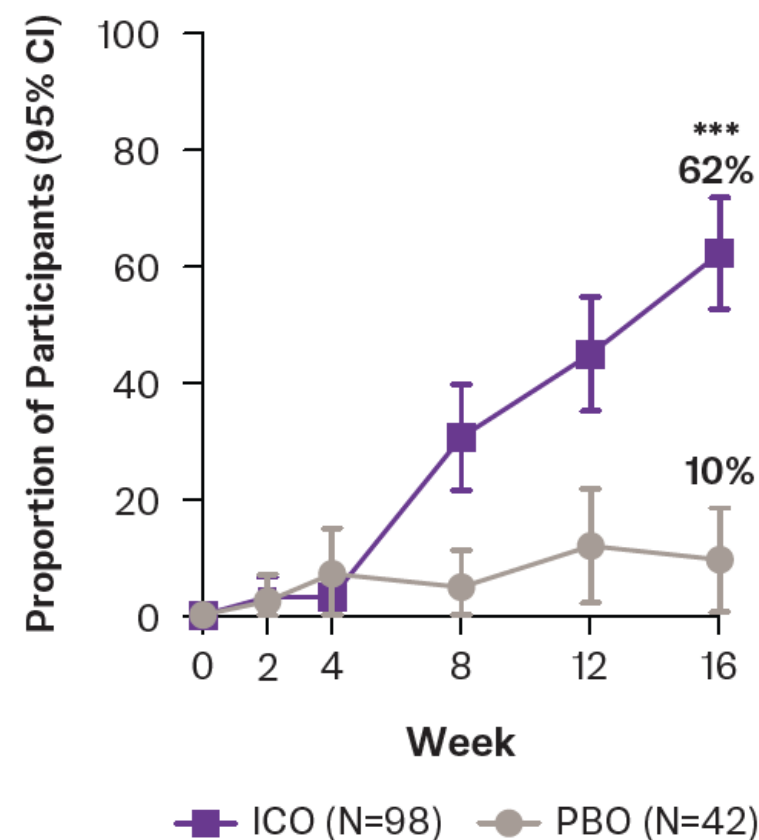
ICO Demonstrated Higher Rates of Completely Clear Scalp and Genital PsO vs PBO

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

Scalp: ss-IGA 0^a



Genital: sPGA-G 0^a



***Nominal P<0.001 vs PBO^b

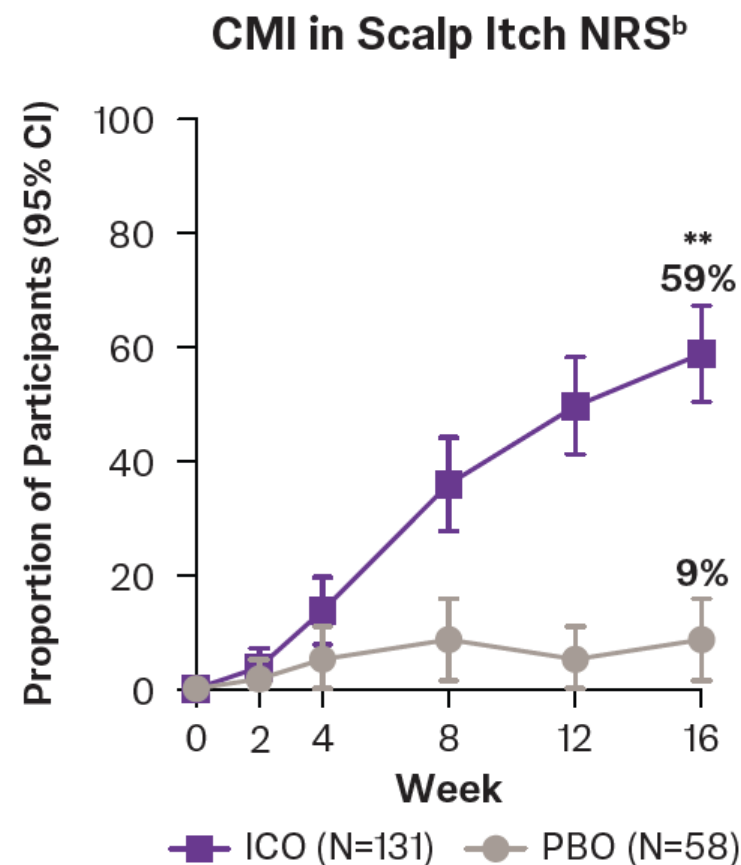
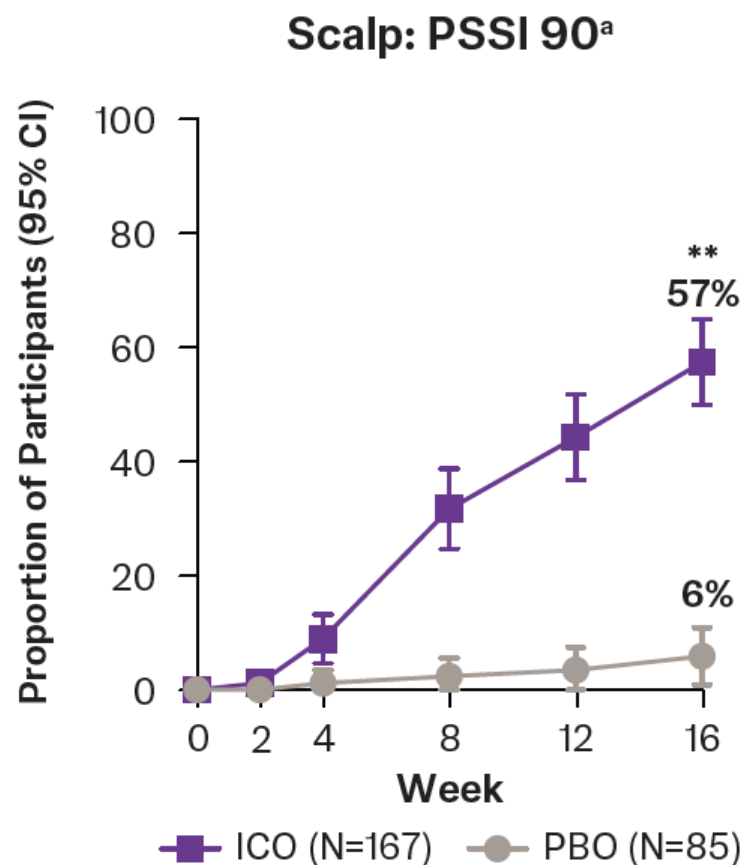
^aAmong pts with a baseline ss-IGA score, sPGA-G score, or hf-PGA score ≥3.

^bP values were based on Cochran-Mantel-Haenszel chi-square test stratified by geographic region and/or BSA category.

2025 SID Meeting: ICONIC-TOTAL—Plaque PsO and Difficult-to-Treat High Impact Sites

ICO Demonstrated Significantly Higher Rates of Scalp Clearance and Meaningful Improvement in Scalp Itch vs PBO

- ICO demonstrated early separation from PBO



***Multiplicity-adjusted $P < 0.001$ vs PBO^c

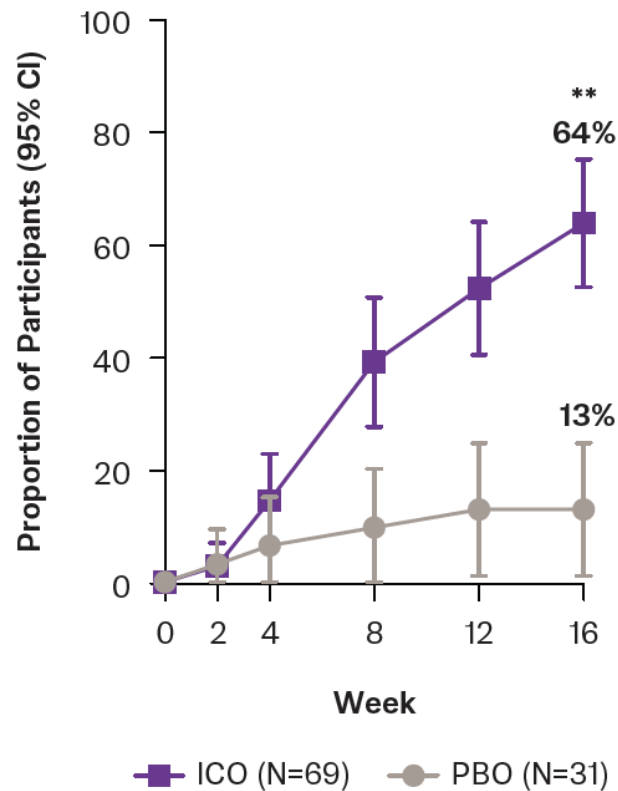
^aAmong pts with a baseline ss-IGA score ≥ 3 . ^bAmong pts with a baseline Scalp Itch NRS score ≥ 4 and a ss-IGA score ≥ 3 . ^cP values were based on Cochran-Mantel-Haenszel chi-square test stratified by geographic region and BSA category. **CMI**=clinically meaningful improvement (≥ 4 -point improvement from baseline); **NRS**=numeric rating scale; **PSSI**=Psoriasis Scalp Severity Index; **PSSI 90**=reduction from baseline of 90% in the PSSI score.

2025 SID Meeting: ICONIC-TOTAL—Plaque PsO and Difficult-to-Treat High Impact Sites

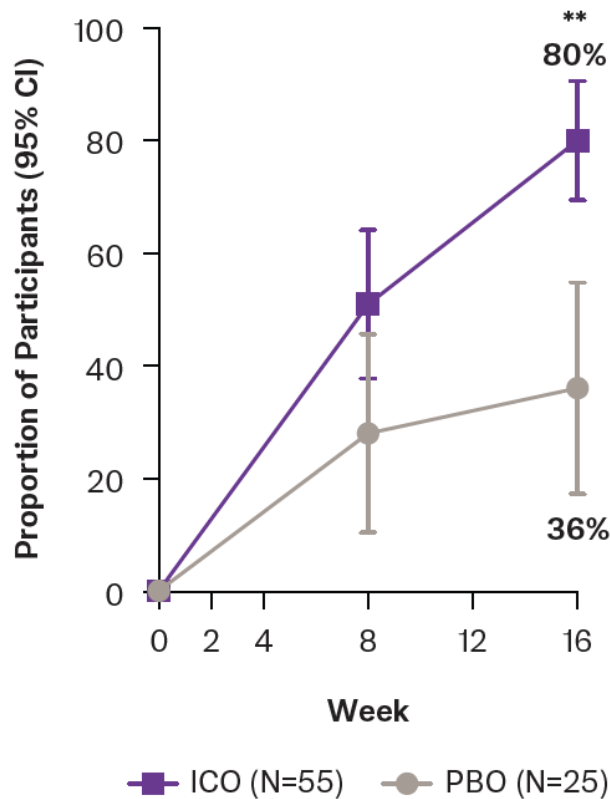
ICO Significantly Improved Pt-Reported Genital PsO Itch & Impact of PsO on Sexual Activity vs PBO

- ICO demonstrated early separation from PBO

CMI in GPSS Genital Itch NRS^a



Genital: GenPs-SFQ 0/1^b



***Multiplicity-adjusted $P < 0.001$ vs PBO^c

^aAmong pts with a baseline GPSS Genital Itch NRS score (Item 1) ≥ 4 and a sPGA-G score ≥ 3 .

^bAmong pts with a baseline GenPs-SFQ score (Item 2) ≥ 2 and a sPGA-G score ≥ 3 .

^cP values were based on Cochran-Mantel-Haenszel chi-square test stratified by BSA category.

CMI=clinically meaningful improvement (≥ 4 -point improvement from baseline); **GenPs-SFQ**=Genital Psoriasis Sexual Frequency Questionnaire; **GPSS**=Genital Psoriasis Symptoms Score.

2025 SID Meeting: ICONIC-TOTAL—Plaque PsO and Difficult-to-Treat High Impact Sites

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 ^a	1 (<1%)	2 (2%)
Infection	59 (28%)	22 (21%)
Serious infection	0	1 (1%)
AE leading to discontinuation ^b	4 (2%)	3 (3%)
Gastrointestinal AEs	15 (7%)	8 (8%)
Active TB	0	0
Malignancy ^c	1 (<1%)	0

^aSAEs through W16 included COVID-19 pneumonia, sepsis, sciatica, and acute respiratory failure in the PBO group; and hepatitis in the ICO group. ^bAEs leading to discontinuation through W16 included COVID-19 pneumonia, psoriatic arthropathy, and psoriasis in the PBO group; and vision blurred, visual field defect, laryngitis fungal, malignant melanoma in situ, and headache in the ICO group. ^cMalignancy reported in the ICO group was malignant melanoma in situ in a pt with a recent personal history of melanoma (in 2021). **COVID-19**=coronavirus disease 2019; **SAE**=serious adverse event; **TB**=tuberculosis.

2025 SID Meeting: ICONIC-TOTAL—Plaque PsO and Difficult-to-Treat High Impact Sites

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 & adolescents with moderate-to-severe plaque PsO⁴

ICONIC-ADVANCE 1 and 2: Head-to-Head Superiority Study vs. Deucravacitinib in Psoriasis

Study Met All Secondary Endpoints Measuring Superiority to Deucravacitinib

Adult Patients with Moderate to Severe Plaque PsO

N=774 (ICONIC-ADVANCE 1) and
N=731 (ICONIC-ADVANCE 2)

Eligibility:

- Adults ≥18 years old
- Plaque PsO, with or without PsA, for ≥26 weeks
- Total BSA ≥10% AND total PASI ≥12 AND total IGA ≥3 at screening and baseline
- Candidate for phototherapy or systemic treatment for plaque psoriasis

Co-primary endpoint:

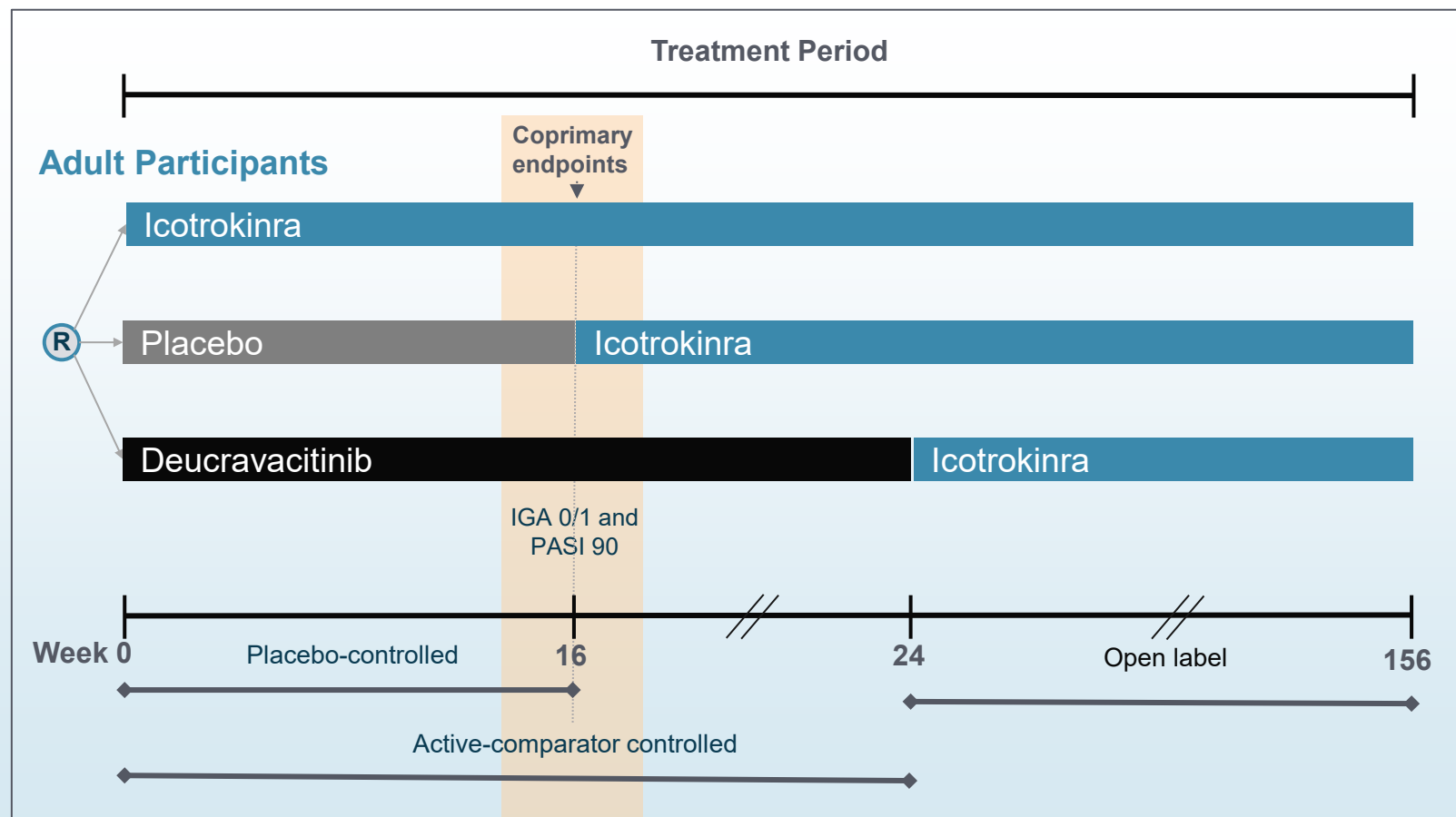
- IGA 0/1 (Week 16) and PASI 90 (Week 16)

Key secondary endpoints:

- 10 key secondary endpoints (eg, PROs) vs. placebo at Weeks 4, 8, and 16
- 11 superiority endpoints (eg, PRO) vs. deucravacitinib at Weeks 16 and 24

Primary completion dates:

- March 2025 (ICONIC-ADVANCE 1) and
November 2024 (ICONIC-ADVANCE 2)



Icotrokinra Clinical Studies Update

- **Phase 3 ICONIC-LEAD study**

- Co-primary endpoints (PASI 90 and IGA 0/1, week 16) met
 - Two-thirds (65%) of treated patients achieved IGA score of 0/1 (clear or almost clear skin) and 50% achieved a PASI 90 response, compared to 8% and 4% receiving placebo, respectively ($P < 0.001$ for both endpoints) at Week 16
 - Continued skin clearance improvement was reported at Week 24 with 74% of patients treated with icotrokinra achieving IGA 0/1 and 65% achieving PASI 90
- **Nearly half of patients treated with icotrokinra achieved completely clear skin – 46% reached IGA 0 and 40% reached PASI 100 at week 24**
- Similar proportions of patients experienced adverse events (AEs) between icotrokinra (49%) and placebo groups (49%), with no new safety signals identified

- **Phase 3 ICONIC-ADVANCE 1&2 studies**

- Co-primary endpoints (IGA 0/1, PASI 90, Week 16) achieved; superiority to deucravacitinib in moderate-to-severe psoriasis established
- All key secondary endpoints also met

- **Phase 3 ICONIC-ASCEND study initiation**

- The first-ever head-to-head study seeking to demonstrate the superiority of an oral pill, icotrokinra, compared to an injectable biologic, ustekinumab

ICONIC-PsA 1 (NCT06878404): Icotrokinra Phase 3 Study in Biologic-naïve Participants With Active Psoriatic Arthritis

Adult Patients with Psoriatic Arthritis

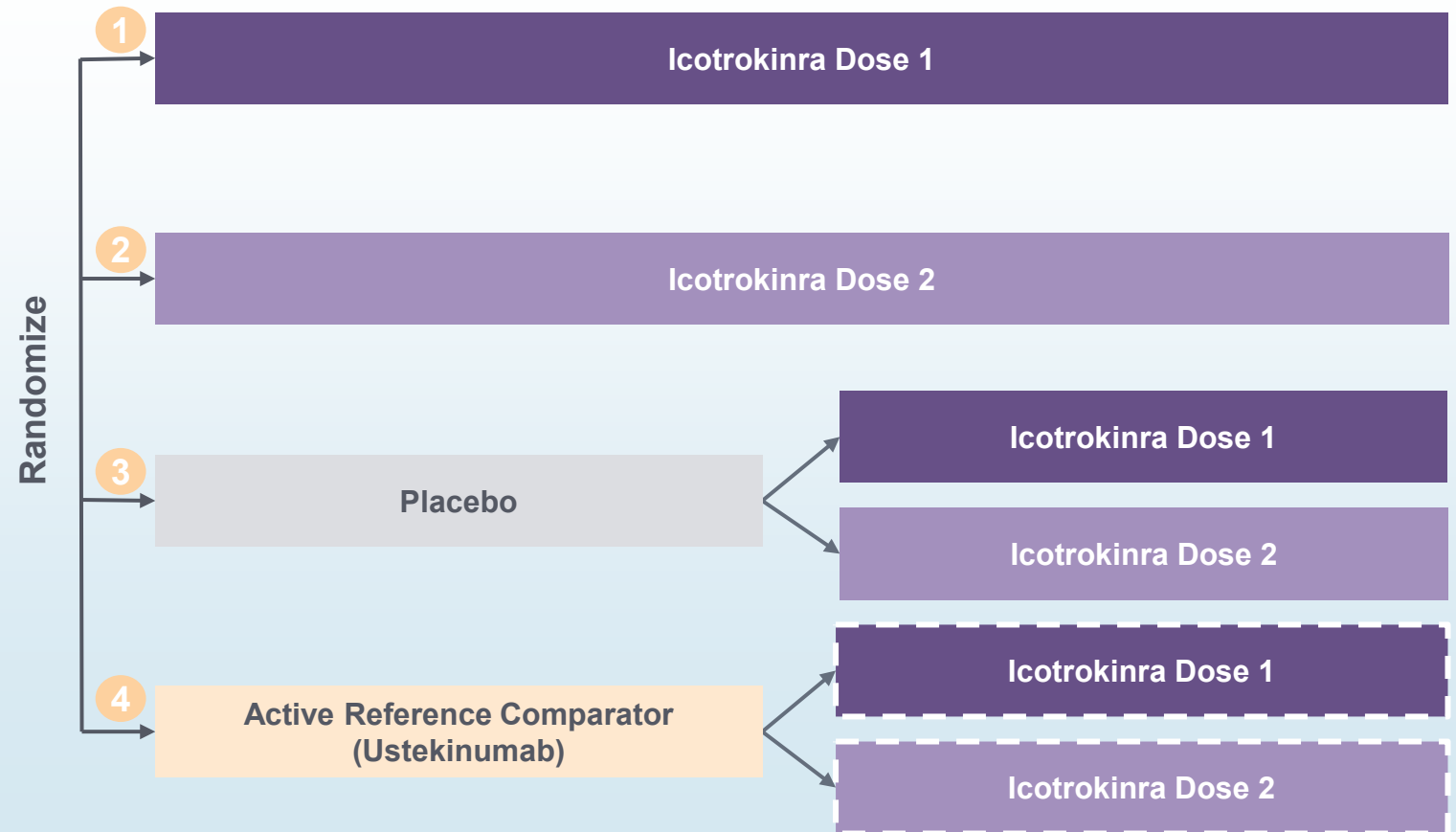
N = 540

Eligibility:

- 18 years of age or older
- Psoriatic Arthritis for >3 months
- Meet classification criteria for psoriatic arthritis (CASPAR) at screening
- Excludes patients who have received any biologic disease-modifying antirheumatic drugs for psoriatic arthritis or psoriasis

Primary endpoint:

- Proportion of patients who achieve an American College of Rheumatology 20 (ACR 20*) Response at Week 16
- Primary completion date: October 2026



ICONIC-PsA 2 (NCT06807424): Icotrokinra Phase 3 Study in Biologic-experienced Participants With Active Psoriatic Arthritis

Adult Patients with Psoriatic Arthritis

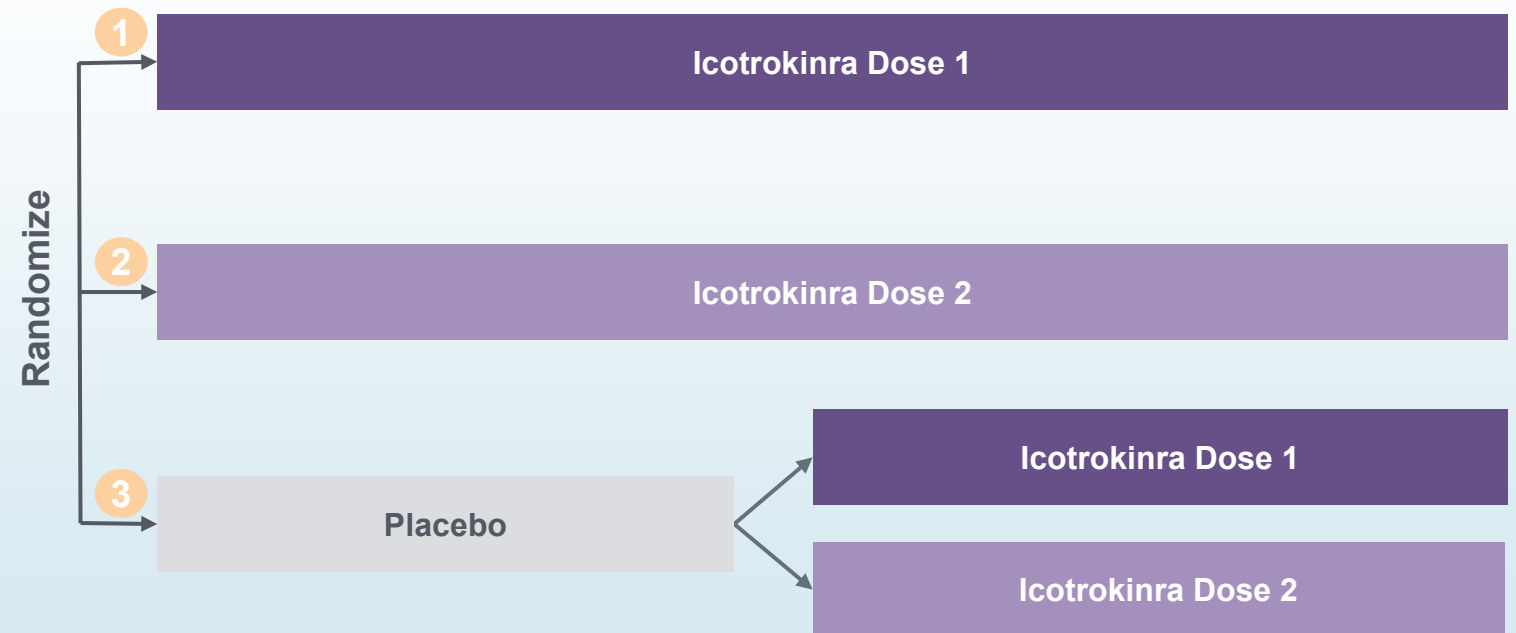
N = 750

Eligibility:

- 18 years of age or older
- Psoriatic Arthritis for >3 months
- Meet classification criteria for psoriatic arthritis (CASPAR) at screening
- Patients must have been previously treated with 1 biologic agent for psoriatic arthritis or psoriasis

Primary endpoint:

- Proportion of patients who achieve an American College of Rheumatology 20 (ACR 20*) Response at Week 16
- Primary completion date: February 2027



ANTHEM-UC (NCT06049017): Icotrokinra (JNJ-2113) Phase 2b Study in Moderate to Severe Ulcerative Colitis (UC)

Adult Patients with UC

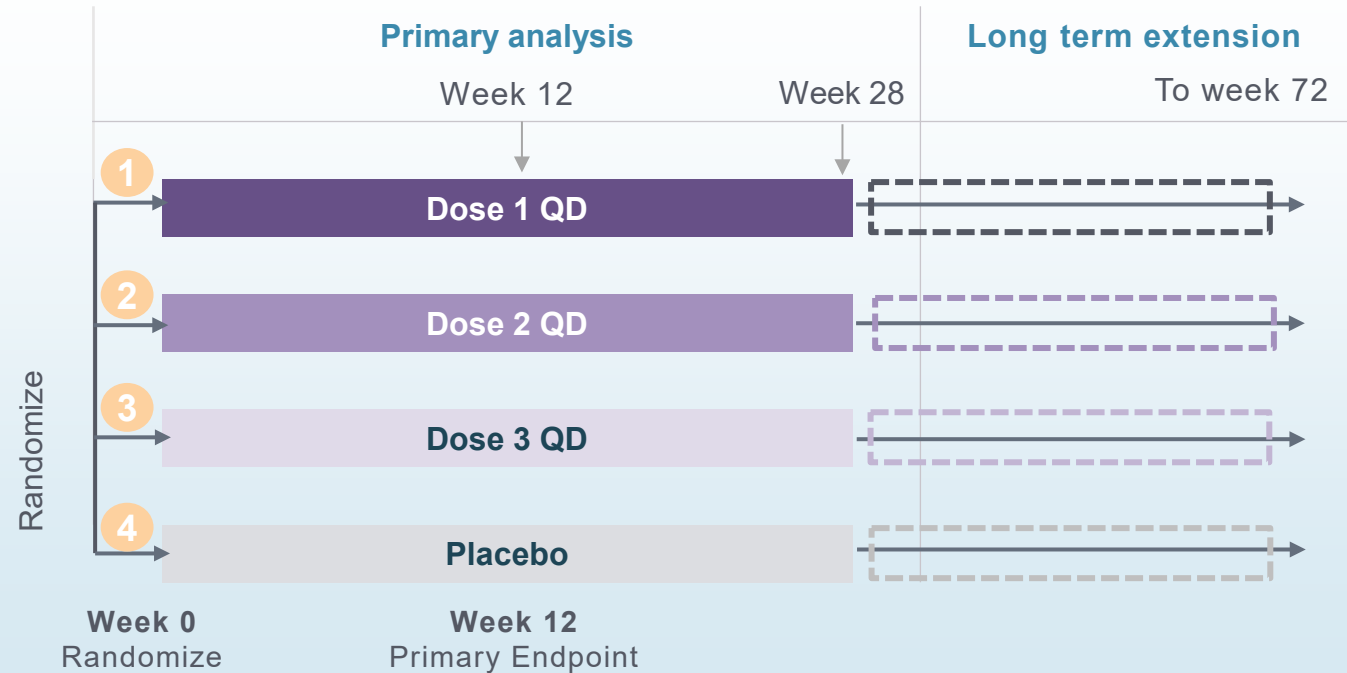
N = 252

Eligibility:

- 18 years of age or older
- Moderately to severely active UC as per the modified Mayo score
- Demonstrated inadequate response to or intolerance of conventional therapy and/or advanced therapy

Primary endpoint:

- Clinical Response (Modified Mayo score) at Week 12
- Primary Completion: 26 September 2024



Icotrokinra Phase 2 ANTHEM-UC Study

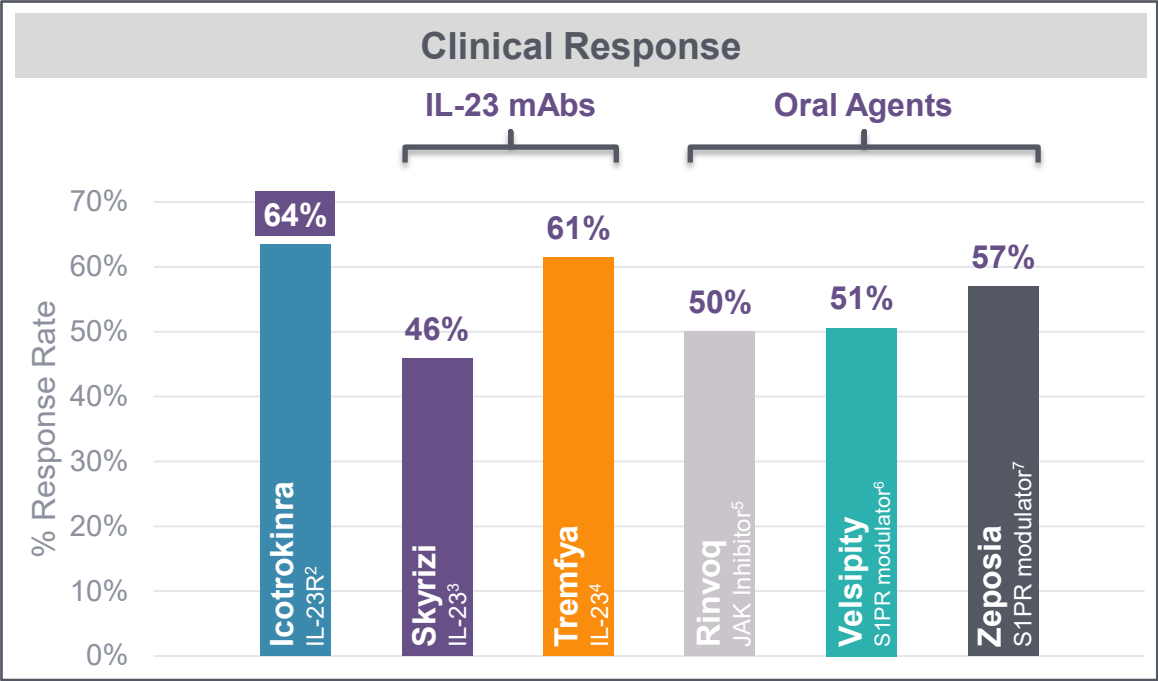
Key Findings

- Positive outcome showing potential to transform UC treatment paradigm
- At week 12, the highest dose achieved
 - 1° endpoint: **Clinical response = 63.5%**
 - 2° endpoint: **Clinical remission = 30.2%**
 - Clinical remission and response rates continued to improve through week 28
- All 3 doses met the primary endpoint of clinical response at week 12, with a favorable safety profile
- Clinically meaningful differences versus placebo in key secondary endpoints of clinical remission, symptomatic remission, and endoscopic improvement at week 12
- **Next steps:** More advanced clinical studies in ulcerative colitis and Crohn's disease

Icotrokinra has the potential to transform the treatment landscape in UC through its distinctive profile of efficacy, safety, tolerability, and convenience of a once-daily oral treatment.

Icetrokinra Cross-Trial Comparison to Phase 2 Benchmarks in UC¹

Clinical Response



Agent	Endpoint Timeframe	Placebo Response (%)
Icetrokinra	Wk 12	27.0
Skyrizi	Wk 12	20.0
Tremfya	Wk 12	27.6
Rinvoq	Wk 8	13
Velsipity	Wk 12	32.5
Zeposia	Wk 8	37

1. Cross trial (not head-to-head) comparisons of unadjusted (ie, non-placebo adjusted) response data from phase 2 studies.

2. Icetrokinra (JNJ-2113) highest dose (in mg; PO qd) with clinical response at Wk 12 (ie, decrease from baseline in the modified Mayo score by ≥30% and ≥2 points, with either a ≥1-point decrease from baseline in the rectal bleeding subscore or a rectal bleeding subscore of 0 or 1). Clinical response (placebo): 27.0%. Protagonist Therapeutics, Inc. “Protagonist Reports Positive Top Line Results from Phase 2b Study of Icetrokinra Showing Potential to Transform the Treatment Paradigm for Patients with Ulcerative Colitis.” News release. 10 March 2025.

3. Skyrizi 1200 mg IV (approved dose; phase 2 data) clinical response per Adapted Mayo score at Wk 12 (ie, decrease of ≥30% and ≥2 points from baseline and a decrease in rectal bleeding score of ≥1 or an absolute rectal bleeding score ≤1). Clinical response score (placebo): 20.0%. Louis E, et al., *JAMA*. 2024;332:881-97.

4. Tremfya 200 mg IV (approved dose; phase 2 data) clinical response at Wk 12 (ie, decrease in modified Mayo score from baseline by ≥30% and ≥2 points, with either a ≥1-point decrease from baseline in the rectal bleeding subscore or a rectal bleeding subscore of 0 or 1). Clinical response (placebo): 27.6%. Peyrin-Biroulet L, et al., *Gastroenterology*. 2022;165:1443-57.

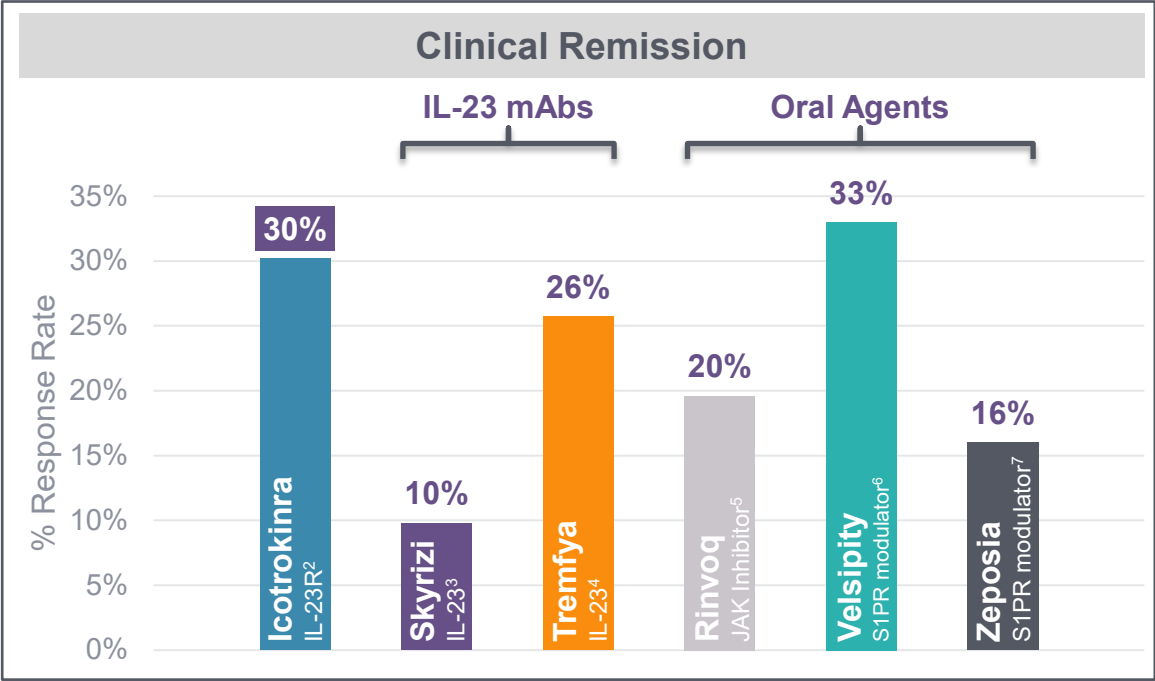
5. Rinvoq 45 mg PO QD (approved dose; phase 2 data) with clinical response at Wk 8 (ie, adapted Mayo score; defined as a decrease from baseline in the adapted Mayo score of 2 points and 30% from baseline, plus a decrease in rectal bleeding score of 1 or an absolute rectal bleeding score of 1). Clinical response (placebo): 13%. Sandborn WJ, et al., *Gastroenterology*. 2020;158:2139-49.

6. Velsipity 2 mg PO QD (approved dose; phase 2 data) with clinical response at Wk 12 (ie, met the criteria for clinical remission or had a decrease in modified Mayo Clinic score of 2 points and a decrease of 30%, with either a rectal bleeding score of 1 or a decrease in rectal bleeding of 1). Clinical response (placebo): 32.5%. Sandborn WJ, et al., *Gastroenterology*. 2020;158:550-61.

7. Zeposia 1 mg PO QD (approved dose; phase 2 data) with clinical response at Wk 8 (ie, reduction in the Mayo Clinic score of ≥3 points and ≥30% from baseline, with a decrease in the rectal-bleeding subscore of ≥1 point or a subscore of ≤1). Clinical response (placebo): 37%. Sandborn WJ, et al., *New Engl J Med*. 2016;18:1754-62.

Icotrokinra Cross-Trial Comparison to Phase 2 Benchmarks in UC¹

Clinical Remission



Agent	Endpoint Timeframe	Placebo Remission (%)
Icotrokinra	Wk 12	11.1
Skyrizi	Wk 12	1.7
Tremfya	Wk 12	9.5
Rinvoq	Wk 8	0
Velsipity	Wk 12	8.1
Zeposia	Wk 8	6

1. Cross trial (not head-to-head) comparisons of unadjusted (ie, non-placebo adjusted) remission data from phase 2 studies.

2. Icotrokinra (JNJ-2113) highest dose (in mg; PO qd) with clinical remission at Wk 12 (ie, Mayo stool frequency subscore of 0 or 1 and not increased from induction baseline, a Mayo rectal bleeding subscore of 0, and a Mayo endoscopy subscore of 0 or 1 with no friability present on the endoscopy). Clinical remission (placebo): 11.1%. Protagonist Therapeutics, Inc. "Protagonist Reports Positive Top Line Results from Phase 2b Study of Icotrokinra Showing Potential to Transform the Treatment Paradigm for Patients with Ulcerative Colitis." News release. 10 March 2025.

3. Skyrizi 1200 mg IV (approved dose; phase 2 data) clinical remission per Adapted Mayo score at Wk 12 (ie, stool frequency subscore ≤1, and not greater than baseline, rectal bleeding subscore =0, and endoscopic subscore ≤1 without the evidence of friability). Clinical remission score (placebo): 1.7%. Louis E, et al., *JAMA*. 2024;332:881-97.

4. Tremfya 200 mg IV (approved dose; phase 2 data) clinical remission at Wk 12 (ie, Mayo stool frequency subscore of 0 or 1 and not increased from induction baseline, a Mayo rectal bleeding subscore of 0, and a Mayo endoscopy subscore of 0 or 1 with no friability present on endoscopy). Clinical remission (placebo): 9.5%. Peyrin-Biroulet L, et al., *Gastroenterology*. 2022;165:1443-57.

5. Rinvoq 45 mg PO QD (approved dose; phase 2 data) with clinical remission at Wk 8 (ie, adapted Mayo score; defined as stool frequency subscore of 1, rectal bleeding subscore of 0, and endoscopic subscore of 1). Clinical remission (placebo): 0%. Sandborn WJ, et al., *Gastroenterology*. 2020;158:2139-49.

6. Velsipity 2 mg PO QD (approved dose; phase 2 data) with clinical remission at Wk 12 (ie, Mayo Clinic endoscopic subscore ≤1 [with absence of friability], rectal bleeding score ≤1, and stool frequency score ≤1, with a frequency decrease of ≥1 point from baseline). Clinical remission (placebo): 8.1%. Sandborn WJ, et al., *Gastroenterology*. 2020;158:550-61.

7. Zeposia 1 mg PO QD (approved dose; phase 2 data) with clinical remission at Wk 8 (ie, Mayo Clinic score ≤2, with no subscore >1). Clinical remission (placebo): 6%. Sandborn WJ, et al., *New Engl J Med*. 2016;18:1754-62.

Icotrokinra Summary

Icotrokinra is the First Targeted Oral Peptide Designed to Selectively Block the IL-23 Receptor



Psoriasis (PsO)

- 4 Phase 3 ICONIC trials in moderate-to-severe plaque psoriasis (PsO)
 - Approximately 65% of patients achieve PASI 90 and approximately 75% of patients achieve IGA 0/1 by Week 24
 - Nearly 50% of patients had completely clear skin (IGA 0) at Week 24
 - Icotrokinra showed superiority vs. deucravacitinib at Weeks 16 and 24 in the proportions of patients achieving PASI 75, 90, 100, IGA 0/1, and IGA 0, as well as no symptoms as measured by PSSD 0
 - Phase 3 ICONIC-TOTAL results in pts with plaque PsO and difficult-to-treat, high-impact site involvement extend results from the ongoing phase 3 ICONIC-LEAD study evaluating icotrokinra in adults & adolescents with moderate-to-severe plaque PsO
- A phase 3 study (ICONIC-ASCEND) of icotrokinra vs. the injectable biologic Stelara is planned

Psoriatic Arthritis (PsA)

- 2 Phase 3 trials in moderate-to-severe PsA have been initiated: ICONIC-PsA 1 in bio-naïve patients and ICONIC-PsA 2 in bio-experienced patients

Ulcerative Colitis (UC)

- Phase 2b ANTHEM-UC study in patients with moderately to severely active UC: Icotrokinra met the primary endpoint of clinical response in all dose groups
 - Clinical response rates of up to 63.5% and clinical remission rates up to 30.2% at week 12 and a favorable safety profile observed in the phase 2b ANTHEM UC study
 - Clinical response and remission rates continued to improve through Week 28

Crohn's Disease (CD)

- Clinical study of icotrokinra in CD is planned

Rusfertide

A Synthetic Mimetic of the Natural Hormone Hepcidin

Addressing Unmet Needs in
Polycythemia Vera



Polycythemia Vera (PV)

Disease Background

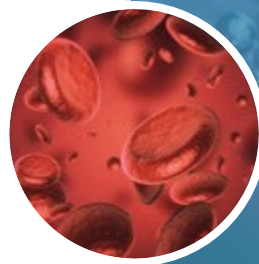
Rare myeloproliferative neoplasm characterized by excessive production of red blood cells (RBCs)¹

- Elevated hematocrit (Hct) >45%²

Serious, chronic disease associated with increased thrombotic and cardiovascular risks¹⁻³

~155,000 PV patients in US, with a median survival of 14 years^{1,5}

1. NORD Rare Disease Database, Polycythemia Vera. <https://rarediseases.org/rare-diseases/polycythemia-vera/>
2. Spivak JL. Ann Hematol 2018; 19(2):1-14
3. Marchioli R, et al. N Engl J Med 2013; 368:22-33
4. Barbui T, et al. Leukemia 2018;32:1057-69
5. Tefferi A, Barbui T. Am J Hematol. 2023;98:1465-87.



Primary Treatment goal is to maintain

Hct < 45%^{3,4}

Polycythemia Vera

Significant Unmet Medical Need

1. Hct Control

- **Maintaining Hct<45% is critical**, as per NCCN guidelines
- **~4 times higher risk of death from uncontrolled Hct¹**

2. Patients

- Up to **78% of patients have uncontrolled Hct $\geq 45\%$ ²**
- **Thrombotic events (34-41%)³⁻⁵**
- **Burdensome symptoms**
 - Fatigue within last 12 months (73%)⁶
 - Full days in bed (23%)⁶
 - Iron deficiency (anemia)⁷

3. Therapy

- **Current standard of care (SOC)**
 - Phlebotomy, hydroxyurea (HU), interferon, Jakafi
 - Inadequate
- **No RBC-specific pharmaceutical option available**

Rusfertide, a hepcidin mimetic, could potentially provide an RBC-specific treatment option for PV

1. Marchioli R, et al. *N Engl J Med*. 2013;368:22-33.

2. Verstovsek S, et al. *Ann Hematol*. 2023;102(3):571-581.

3. Kaifie A, et al. *J Hematol Oncol*. 2016;9:18.

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5. Polycythemia vera: the natural history of 1213 patients followed for 20 years. Gruppo Italiano Studio Policitemia. *Ann Intern Med* 1995;123(9):656-64.

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Identifying PV Patients with Moderate Treatment Burden



Defining the “moderate treatment burden” population using current market treatments and trends is the key to understanding rusfertide's market opportunity

Key indicators of suboptimal control for a PV patient

Phlebotomy Frequency



A high frequency of phlebotomies indicates the intervention is not working to maintain Hct $\leq$ 45%

Frequent phlebotomies may exacerbate iron deficiency and related symptoms¹

Dosing of Hydroxyurea



High doses of HU (1-2 g/day) can indicate difficult-to-control PV, especially when used in combination with phlebotomy

Potential serious side effects and adverse events, including leukemic transformation and skin malignancies²

Thrombotic Events



Occurrence of thrombotic events following treatment initiation can be an indicator of the ineffectiveness of the treatment – an example of a sub-optimally controlled PV patient

Marketed Agents for PV are Cyto-reductive Therapies

No Approved Medications That Specifically Target Red Blood Cells and Hematocrit



Interferon

Pegasys®, Besremi®

Interferons have long been used off-label in PV treatment; Besremi is the first interferon product approved for PV¹

Slow onset of action, with average time to response of **1.2 to 1.4 years**²

Failed to show noninferiority to HU at 12 months in the PROUD-PV study³

Black box warning for serious neuropsychiatric, autoimmune, ischemic, and infectious disorders²



Ruxolitinib

Jakafi®

Only approved for hydroxyurea-resistant or intolerant patients⁴

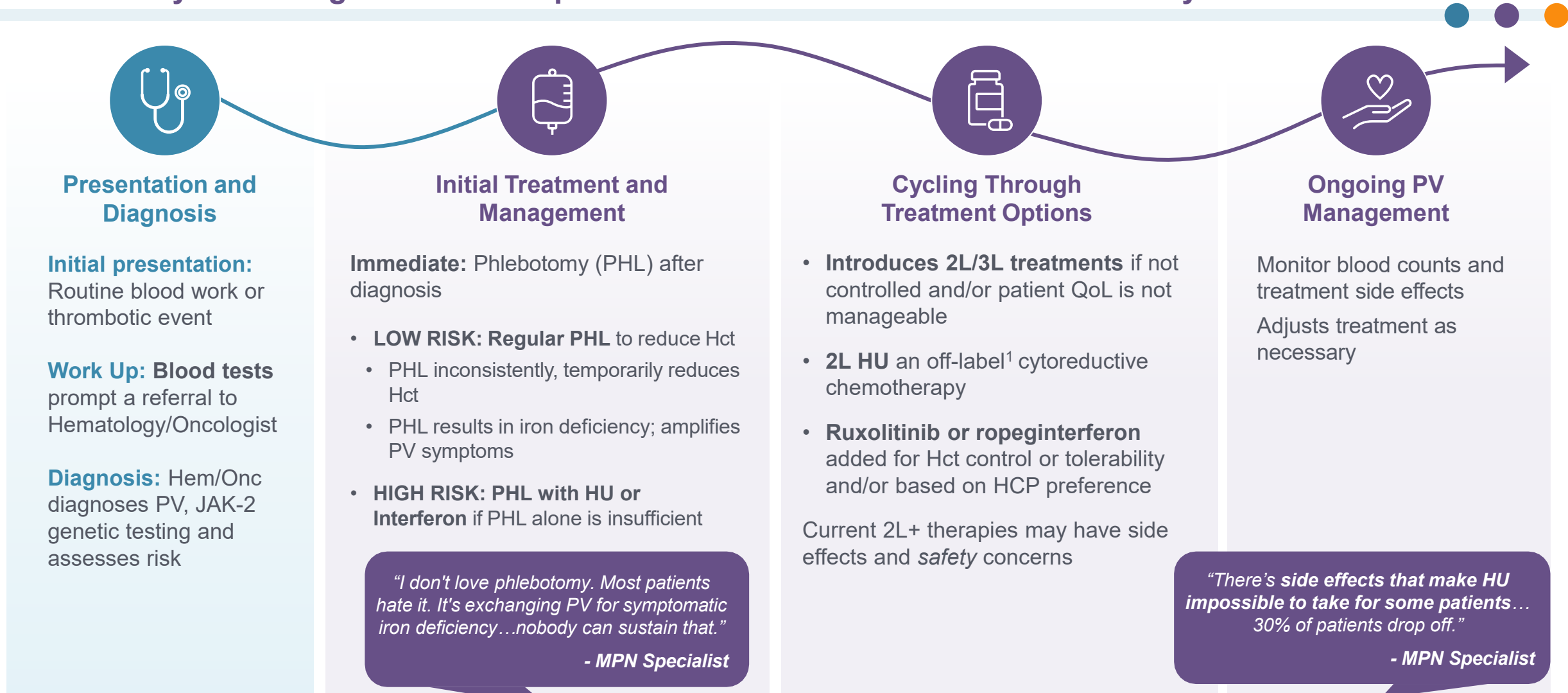
Improves splenomegaly, a potential marker of disease progression⁵

Potential serious side effects include thrombocytopenia, neutropenia, and anemia⁴

23% of patients were found to have discontinued ruxolitinib within a mean of **2 years** post treatment initiation⁶

Patient Journey in PV Identifies Unmet Need in Current Treatment Paradigm

Patients Cycle Through Treatment Options with Inconsistent Hct and Tolerability



HCPs also educate patients on lifestyle modifications, symptom surveillance, and treatment adherence through the management of PV

Polycythemia Vera (PV)

Rusfertide Clinical Development Program

- PV is a rare myeloproliferative neoplasm characterized by excessive production of red blood cells¹
 - Elevated hematocrit (Hct) >45%²
 - Primary treatment goal is to maintain Hct <45%^{3,4}

HEMATOLOGY	 RUSFERTIDE Hepcidin Mimetic	Discovery/Pre-Clinical	Phase 1	Phase 2	Phase 3	Key Milestones
		Polycythemia Vera (PV)				
		VERIFY Ph 3, n=293				• Topline 32-Wk Primary EP results ✓
		REVIVE Ph 2, n=70				• Completed ✓
		THRIVE LTE, n=46				• Ongoing; for REVIVE patients in OLE ✓
		PACIFIC Ph 2, Elevated Hct (>48%), n=20				• Completed ✓

Rusfertide has **Orphan Drug** designation and **Fast Track** status for PV

Rusfertide Phase 3 **VERIFY** Study

Clinical Study Design and Topline Results

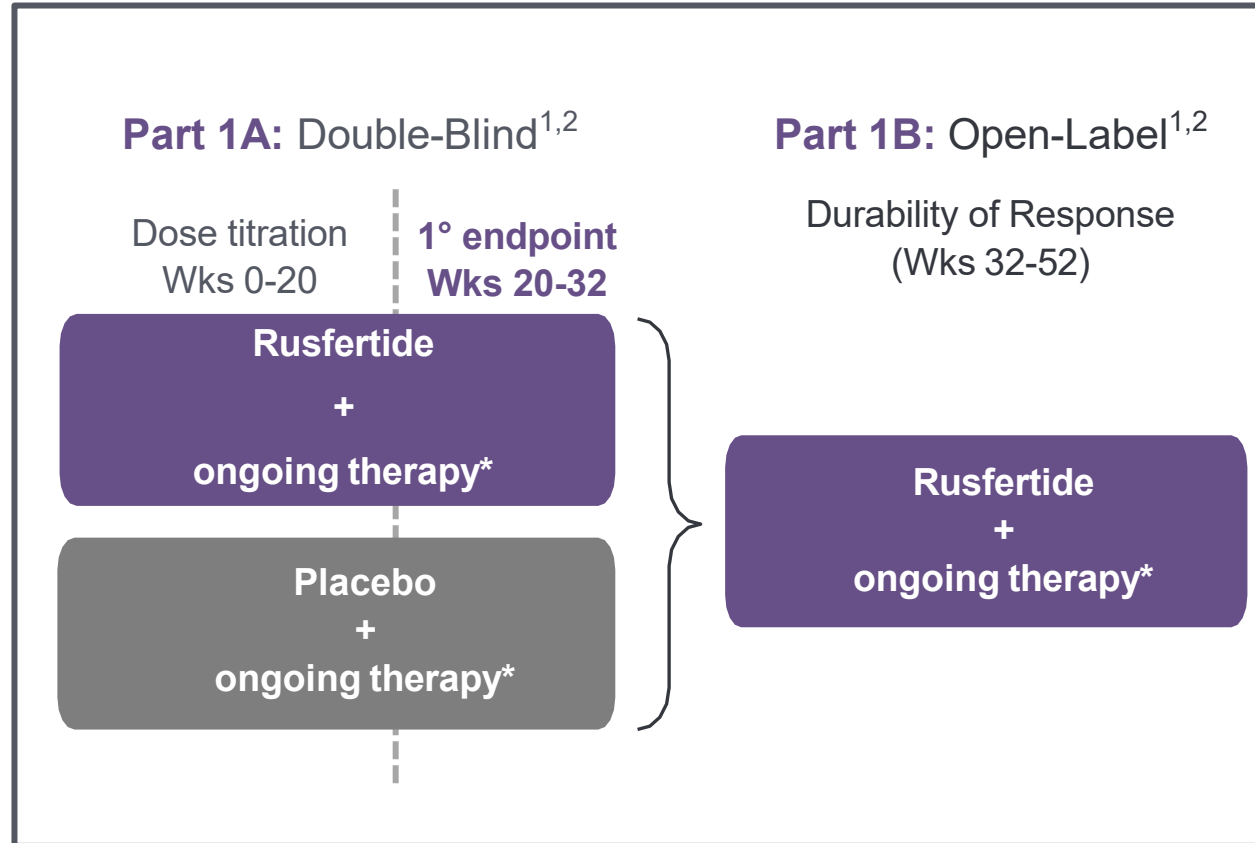
ASCO 2025
Plenary
Session

Inclusion Criteria

≥3 PHL (28 wks prior)
OR
≥5 PHL (1 year prior)

N = 293

1:1 randomization



Primary endpoint:³ Wks 20-32

1. Clinical Response: rusfertide vs placebo (p<0.0001) ✓

Key 2° endpoints: Wks 0-32

1. Average number of PHLs⁴ (p<0.0001) ✓

2. Proportion of patients with Hct <45% (p<0.0001) ✓

3. Average PROMIS Fatigue SF-8a Score⁵ ✓

4. Average MFSAF Total Symptom Score⁶ ✓

*Ongoing therapy could include therapeutic phlebotomy and/or cytoreductive therapy.

1. ClinicalTrials.gov. NCT05210790. <https://clinicaltrials.gov/ct2/show/NCT05210790>;

2. ASCO'24: Bankar A, et al. VERIFY: A randomized controlled phase 3 study of the hepcidin mimetic rusfertide (PTG-300) in patients with polycythemia vera (PV). J Clin Oncol;2024;42;16_suppl. TPS6592.

3. US primary endpoint

4. EU primary endpoint

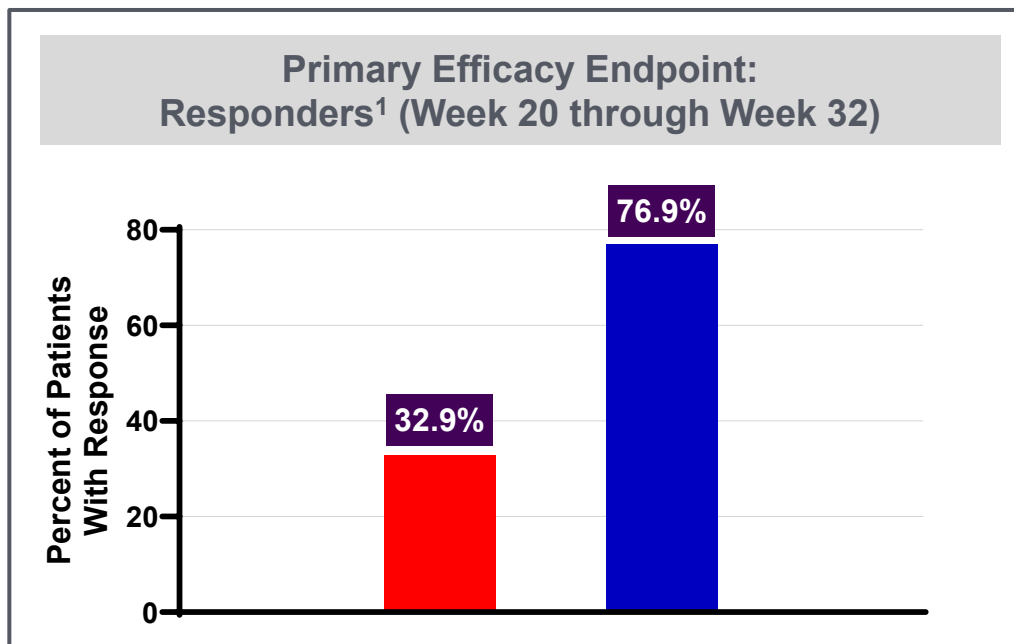
5. Garcia SF, et al. J Clin Oncol. 2007;25:5106-12; Cella D, et al. J Clin Epidemiol. 2016;73:128-34

6. Mesa RA, et al. Leuk Res. 2009;33:1199-203; Gwaltney C, et al. Leuk Res. 2017;59:26-31

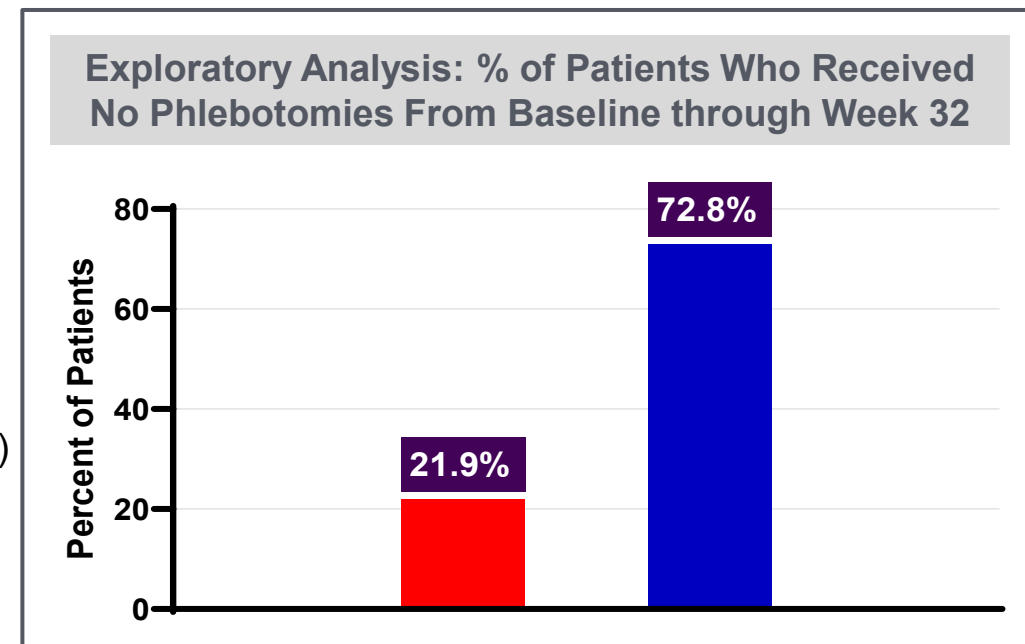
VERIFY: Primary and First Key Secondary Endpoint Met ($p < 0.0001$)

Phlebotomy Eligibility (Weeks 20-32) and Mean Number of Phlebotomies (Baseline through Week 32)

- First Key Secondary Endpoint: Mean number of phlebotomies per patient during weeks 0-32
 - Rusfertide arm, 0.5; placebo arm, 1.8; $p < 0.0001$



■ Placebo (N=146)
■ Rusfertide (N=147)



¹ Definition of “clinical response”:

- completed weeks 0-32 of the study
- was not phlebotomy eligible during weeks 20-32
- did not receive a phlebotomy during weeks 20-32

VERIFY: Other Secondary Endpoints Also Achieved With Statistical Significance

- Hematocrit control¹
- Patient-reported outcome: PROMIS Fatigue SF-8a²
- Patient-reported outcome: MFSAF TSS-7³

¹ Proportion of patients with hematocrit <45%

² Mean change from baseline to week 32 using PROMIS Fatigue SF-8a, a questionnaire that measures patient-reported fatigue symptoms and their impact on daily life

³ Mean change from baseline to week 32 using MFSAF TSS-7 version 4.0, a questionnaire that measures patient reporting of seven key symptoms related to myelofibrosis (many of which are common among PV patients as well), including night sweats, pruritus (itching), abdominal discomfort, pain under ribs on left side, fatigue, early satiety (feeling of fullness) and bone pain

VERIFY: Overall Summary of Adverse Events (Weeks 0-32)

- Rusfertide was generally well tolerated
- Safety data were in line with other rusfertide clinical studies; no new safety findings were observed
- Majority of adverse events were grade 1-2 injection site reactions
- All serious adverse events reported were deemed to be not drug-related
- **No evidence of increased risk of cancer in rusfertide-treated patients compared to placebo**

VERIFY: Primary Efficacy and Safety Analysis

Conclusions

- Study met primary endpoint with a significantly higher proportion of clinical responders on rusfertide compared to placebo during weeks 20-32 ($p < 0.0001$)
- Study met all four key secondary endpoints (weeks 0-32)
 - Phlebotomy rate - EU primary endpoint ($p < 0.0001$)
 - Hematocrit control
 - Patient-reported outcomes of PROMIS Fatigue and MFSAF TSS-7
- Safety profile consistent with previous rusfertide studies, with no new safety signals

Rusfertide for Polycythemia Vera

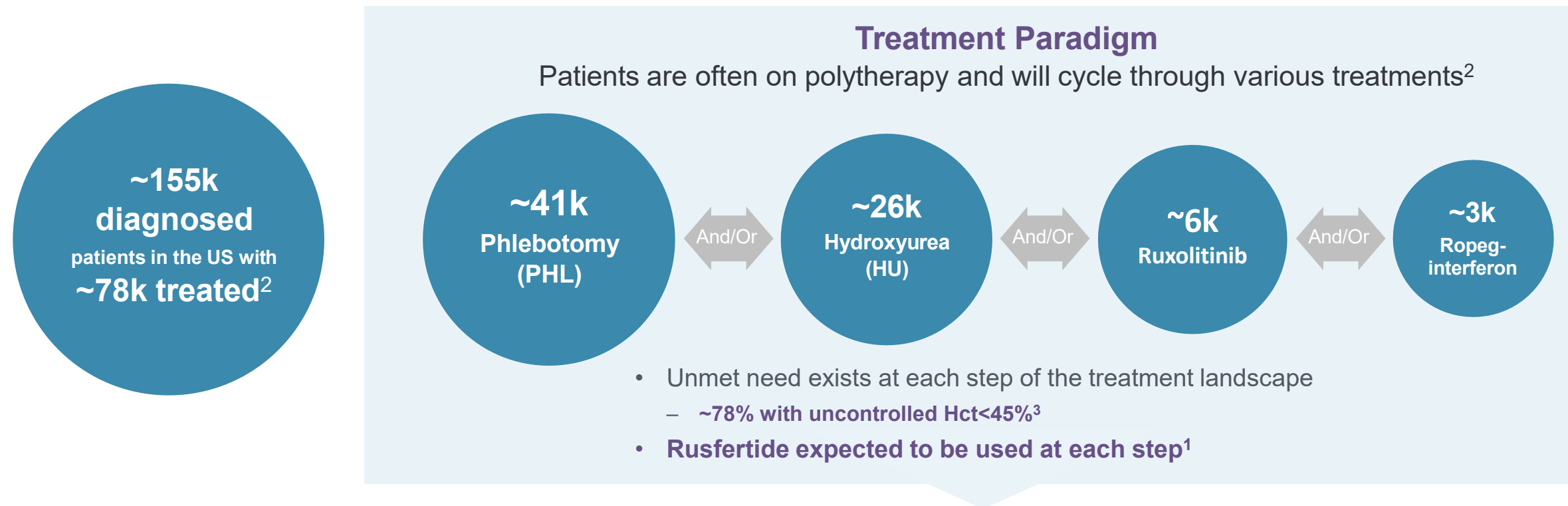
Successful Completion of Phase 2 and 3 Studies

- Phase 2 **REVIVE** Study (N=70):
 - Randomized withdrawal data presented at EHA 2023¹ (late-breaking oral presentation); data published in *NEJM*²
 - Long-term extension data presented at ASH 2023³ and EHA 2024;⁴ final data presented at ASH 2024⁵
 - Full Analysis Population: 69.2% responder rate (vs. 14.8% placebo; $p < 0.0001$)⁵
 - Randomized Analysis Population: 60% responder rate (vs. 13.8% placebo; $p = 0.0004$)⁵
- Phase 2 **THRIVE** Study (N=46):
 - Long-term extension study (for REVIVE patients on study years 3-5)
- Phase 2 **PACIFIC** Study (N=20)⁶:
 - High hematocrit (Hct >48%); 52-week open-label study completed in Q2 2023
- Phase 3 **VERIFY** Study (N=293)^{7,8}
 - Primary endpoint and all four key secondary endpoints achieved in March 2025
 - Data will be presented at key medical meetings in 2025 and included in regulatory filings (eg, NDA, MAA)

Rusfertide has **Orphan Drug** designation and **Fast Track** status for PV

Polycythemia Vera: Prevalence and Treatment Paradigm

Uncontrolled Hematocrit Exists at Each Step of Treatment

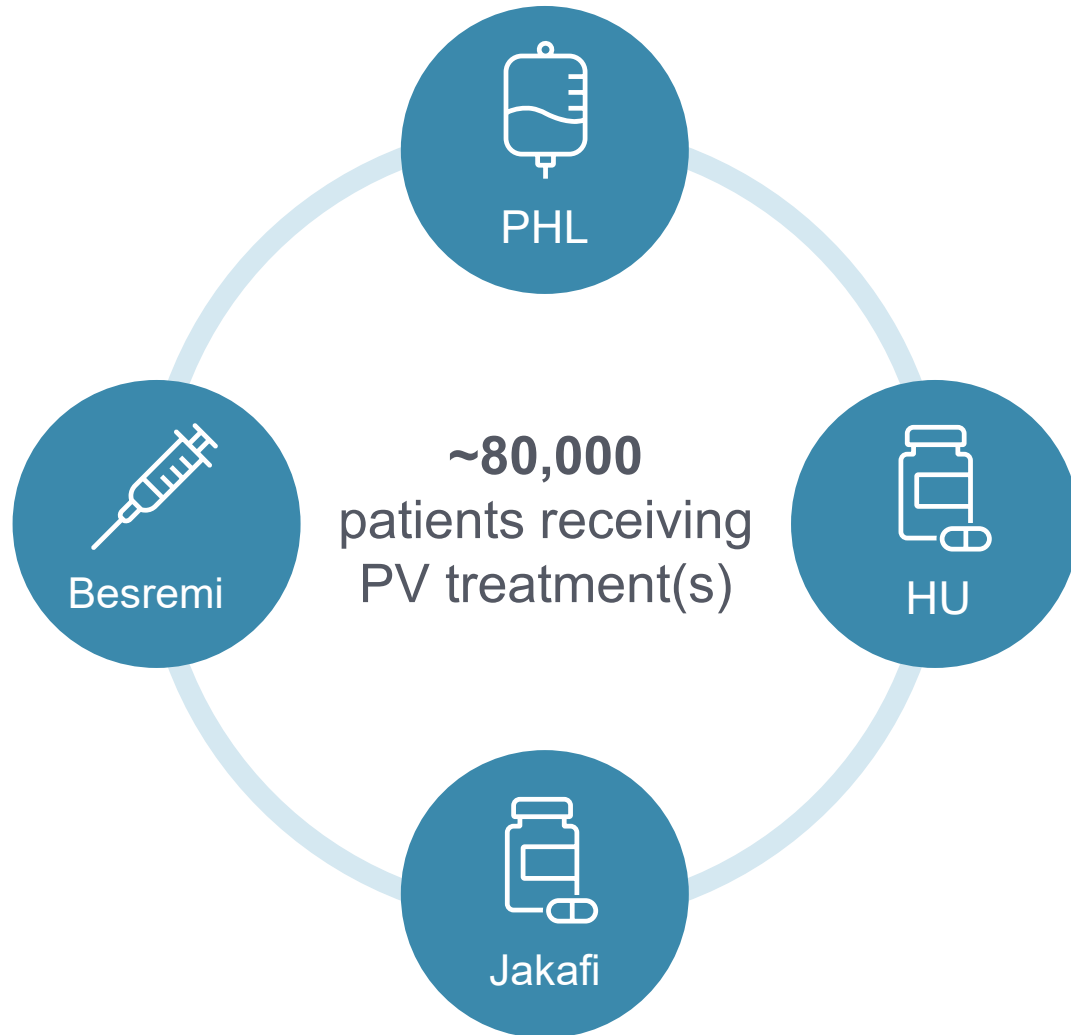


Rusfertide may provide consistent hematocrit control and reduce treatment burden to achieve peak revenue potential of \$1-2B



Rusfertide has \$1-2 Billion Peak Revenue Potential¹

Rapid, Consistent and Sustained Hematocrit Control in a Broad Spectrum of PV Patients



- Rusfertide is the only RBC-specific pharmaceutical therapy that can be used as a monotherapy or combination therapy
- Rusfertide may be utilized at every step of the treatment paradigm to provide consistent, durable hematocrit control
 - Over 75% of patients on current SoC therapies experience HCT $\geq 45\%$, despite receiving treatment
- First agent in PV to demonstrate a statistically significant improvement in symptom burden
- Potential for translation to large commercial opportunity

Oral Hepcidin

- Patients prefer oral medications
- Novel and potent leads with pre-clinical POC
- Several conditions (including hereditary hemochromatosis) cause iron hyperabsorption and dysregulation
- An oral hepcidin agonist would:
 - Target ferroportin in the enterocytes of the small intestine (duodenum), splenic macrophages, and hepatocytes
 - Offer an option for daily oral medication, which may be preferred by some patients
 - Allow treatment of patients earlier in the disease

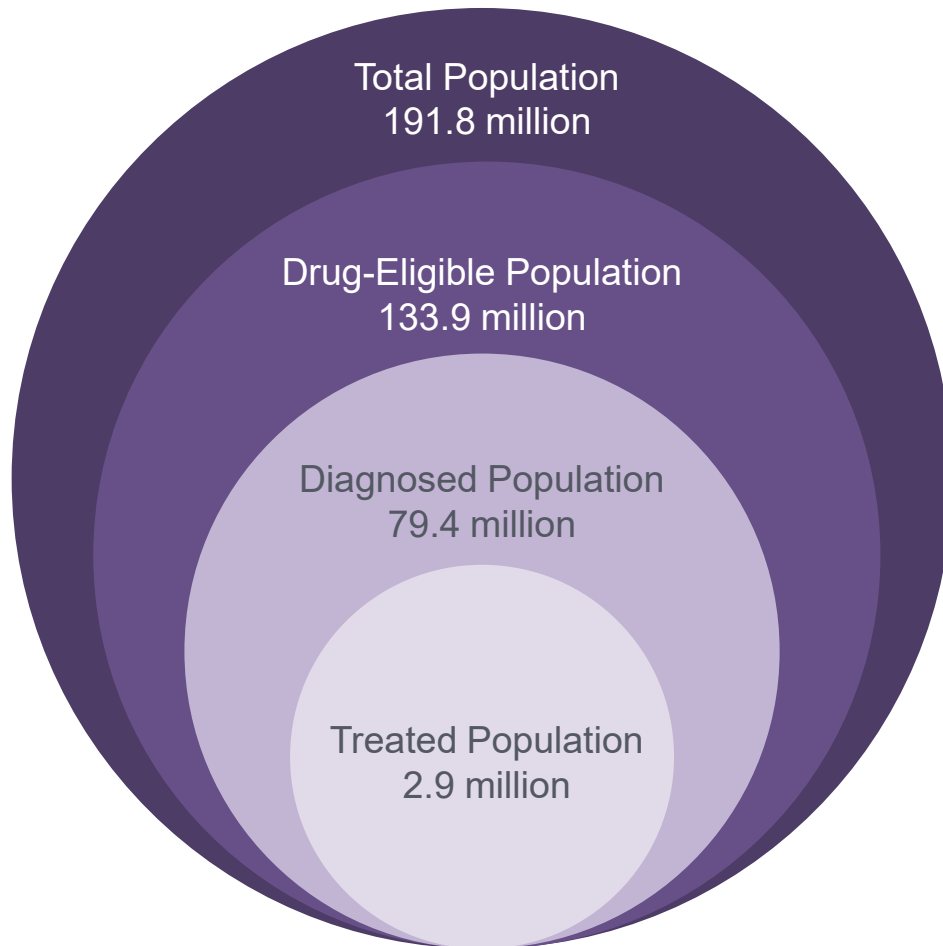
Oral Anti-Obesity Peptides

Huge Unmet Need Remains in Addressing the Obesity in the US and Worldwide

Despite the Rise of GLP-1RA Medications, Less Than 4% of Drug-Eligible Patients Receive Treatment



US Prevalence of Overweight & Obesity¹



- Obesity is a global epidemic
 - Global obesity rates in adults have more than doubled since 1990²
 - In 2024, nearly 40% of Americans had obesity or were considered drug-eligible overweight¹
- Among 191.8 million patients in the US¹:
 - **43%** are overweight ($25 \leq \text{BMI} < 30 \text{ kg/m}^2$)
 - **31%** have obesity, class I ($30 \leq \text{BMI} < 35 \text{ kg/m}^2$)
 - **15%** have obesity, class II ($35 \leq \text{BMI} < 40 \text{ kg/m}^2$)
 - **11%** have obesity, class III ($\text{BMI} \geq 40 \text{ kg/m}^2$)
- Relatively small proportion of patients are treated due to suboptimal cost-effectiveness of current anti-obesity drugs¹
 - Reimbursement challenges and high OOP costs pose barriers for prescribing physicians and patients

Impact of Obesity on Employers

Adult Americans who
are Overweight or Obese¹



Percent of adults age 20+
with obesity = 42.5%;
adults age 20+ who are
overweight, including
obesity = 73.6%

Direct Health
Care Costs²



46% increase in inpatient
costs; 27% increase
in outpatient costs;
80% increase in Rx
costs (vs those of
normal weight)

Lost Productivity
Costs²



Estimated impact beyond
medical claims and health care
utilization in U.S.; costs are a result
of work loss related to absenteeism
and presenteeism, disability and
Workers' Compensation

Greatest Contributor of
Chronic Diseases in U.S.²



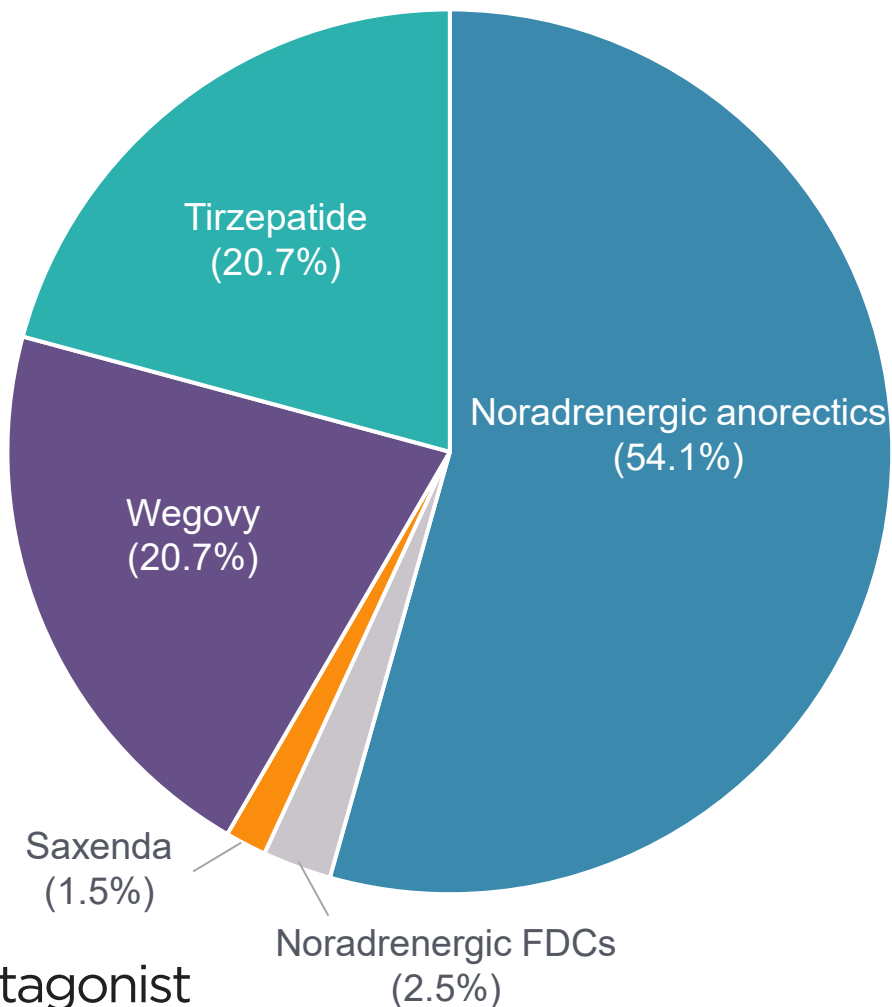
At least 60 comorbidities
and 13 cancers are
attributed to obesity
accounting for 47% of total
costs nationwide

GLP-1 Receptor Agonists To Dominate the Obesity Market By 2033

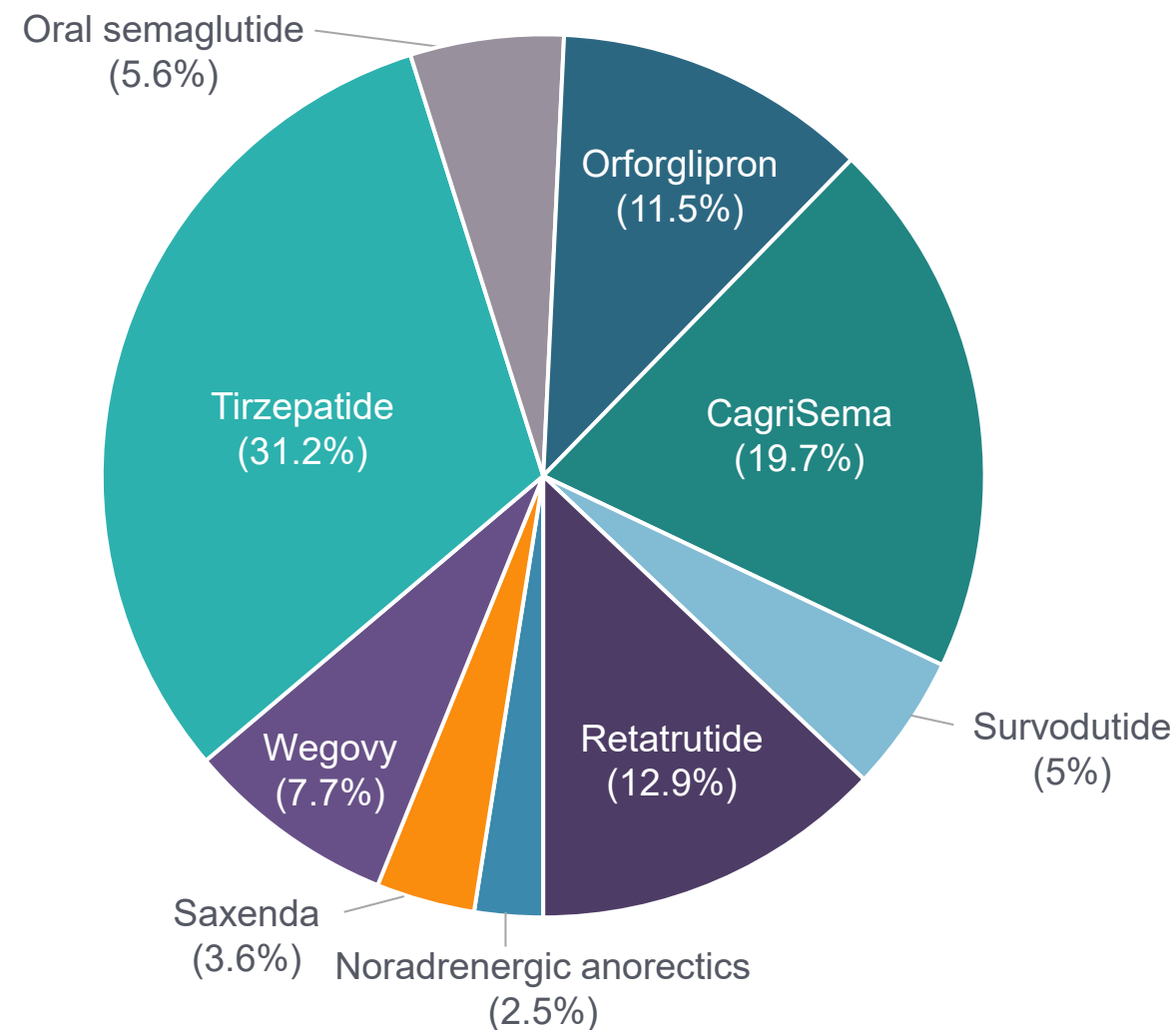
Novel Combination Agonists and Oral Agents Anticipate High Market Penetration



2024 Patient Share



2033 Patient Share



Protagonist Strategy to Improving on Current Injectable Incretin-Based Therapies with Oral Peptide Incretin- and Non-Incretin Agonists

Orally administered incretin and non-incretin peptide therapeutics address important unmet needs

Current therapeutic landscape:

- Two injectable GLP-1RA-based therapies currently approved offer **15-21% mean weight loss** over 68-72 weeks of treatment^{1,2}
- GLP-1RA **tolerability issues** affect treatment persistence^{3,4}
 - Significant **GI side effects**, including nausea, vomiting, constipation, diarrhea^{3,4}
 - Approximately **50%** of patients treated for obesity **discontinue treatment** within the first year of therapy⁵

>

Key areas of focus:

- **Orally** delivered **peptide** therapeutics to improve patient convenience, a significant unmet need
- Focusing on **oral mono- and poly-incretin and non-incretin agonists**
- Improve **magnitude of weight loss**
- Achieve weight loss targets with **fewer adverse side effects**
- Improve **treatment of underlying co-morbidities** while treating obesity
- **Leverage peptide potency** to achieve efficacy with lower doses thereby lowering manufacturing burden

Major Upcoming Catalysts in 2025

Expected Clinical Trial Initiations, Data Readouts and Development Candidate Nominations

	2024	Q1 2025	Q2 2025	2H 2025
	❖ <i>New Engl J Med</i>, 2024; 390:723-35, REVIVE Ph2 ❖ Ph3 VERIFY enrollment completion	❖ PV day¹ ✓ ❖ Topline results² ✓	❖ ASCO plenary session	❖ NDA filing⁴
	❖ <i>New Engl J Med</i>, 2024; 390:510-21, FRONTIER 1 Ph2 results ❖ Ph3 PsO LEAD ✓ ❖ Ph3 PsO TOTAL ✓	❖ Medical Conferences ❖ Ph2b UC ANTHEM² ✓ ❖ Ph3 ICONIC-PsA 1 Initiation² ✓ ❖ Ph3 ICONIC-PsA 2 Initiation² ✓ ❖ Ph3 PsO ADVANCE 1³ ✓ ❖ Ph3 PsO ADVANCE 2³ ✓ ❖ Ph3 PP/EP study³		❖ Psoriasis NDA filing⁴ ❖ Ph3 ICONIC-ASCEND H2H vs. Stelara ❖ New UC study ❖ New Crohn's study
	1. PN-881 ✓ - Oral IL-17 Antagonist Development Candidate (DC)		2. Oral Obesity DC³	❖ Ph1 initiation⁴ 3. Oral Hepcidin DC⁴

Thank you