



COMPANY OVERVIEW

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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 PN-881, obesity, 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), 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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A Peptide Therapeutics Company

Protagonist Therapeutics

- Biologically and commercially validated targets
 - Immunology & inflammation, hematology, and metabolic diseases
- Strong differentiation vs existing therapies

Peptide Technology Platform

**Oral
Hepcidin
Program**

Preclinical

PN-477o
Oral
Triple Agonist
Anti-Obesity
DC

IND-Enabling

PN-477sc
Weekly sc
Triple Agonist
Anti-Obesity
DC

PN-881
Oral
IL-17 Antagonist

Phase 1

Rusfertide
SC Weekly
Hepcidin Mimetic
PV, Ph3



*NDA: PV
~EOY '25*

Icotrokinra
Oral IL-23r
Antagonist

**Johnson&Johnson
Innovative Medicine**

*NDA: Psoriasis
Ph 3: PsA, UC, CD*

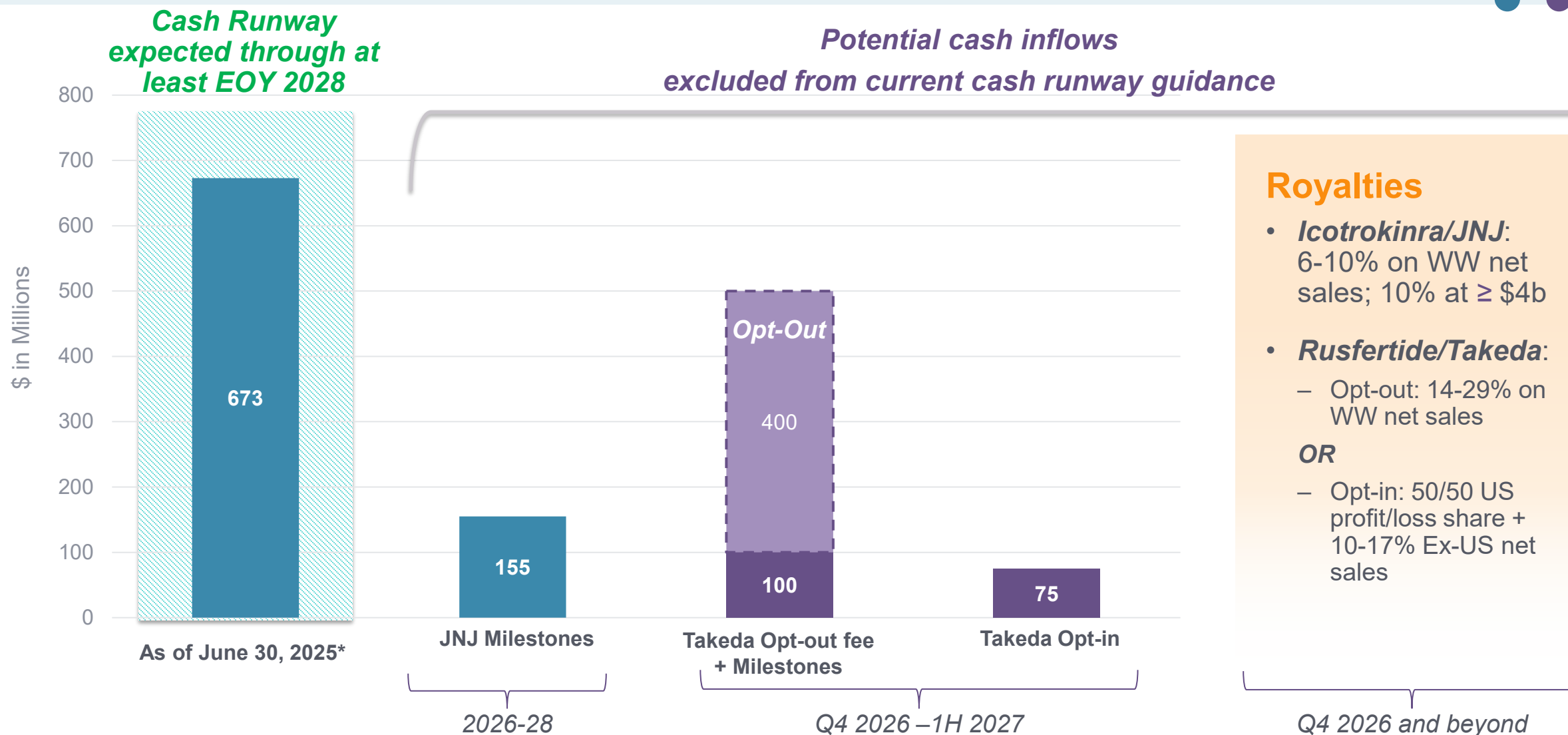
Pipeline of Proprietary and Partnered Programs

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					Psoriasis NDA (US)/MAA (EU) submitted
		ICONIC-LEAD Ph3 completed**, ICONIC-TOTAL Ph3 completed**					
		ICONIC-ADVANCE-1&2 Ph3 completed**, ICONIC-ASCEND Ph3 ongoing					Superiority of icotrokinra vs. deucravacitinib achieved; study of icotrokinra vs ustekinumab initiated
		Psoriatic Arthritis					
		ICONIC PsA-1 & -2 Ph3 ongoing					
		Ulcerative Colitis					
HEMATOLOGY	PN-881* Oral IL-17 Antagonist	Psoriasis, Psoriatic Arthritis, Hidradenitis Suppurativa, Spondyloarthritis					- ICONIC-UC initiated Q4 '25 - ICONIC-CD initiated Q4 '25
		Ph1 initiated					Phase 1 initiated Q4 '25
METABOLIC	Rusfertide SC Hepcidin Mimetic 	Polycythemia Vera					- NDA filing EOY '25 ASCO '25 plenary session
		REVIVE Ph2 completed***, THRIVE Ph2 ongoing, PACIFIC Ph2 completed***, VERIFY Ph3 completed**					
		Polycythemia Vera, Hereditary Hemochromatosis, Other					Development candidate Q4 '25
		Pre-clinical					
METABOLIC	PN-477sc* PN-477oral* Oral GLP-1, GIP, and GCP Agonist	Obesity & Associated Co-Morbidities					- PN-477sc Phase 1 initiation 1H '26 - PN-477oral Phase 1 initiation 2H '26
		IND-Enabling Studies					
		IND-Enabling Studies					

*Fully owned by Protagonist Therapeutics, Inc.; **Primary endpoint completed; ***Study completed.

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
 - Anti-obesity peptide(s)
 - Oral hepcidin mimetic/ferroportin blocker
 - New targets where peptides offer 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
- **\$75M** (opt-out) **or** **\$50M** (opt-in) upon NDA approval

Financial Highlights

Financial Resources Forecast Extends Through At Least Q4 2028

CASH,
CASH EQUIVALENTS &
MARKETABLE SECURITIES

\$672.9M

as of
June 30, 2025

CASH RUNWAY
FORECAST THROUGH
AT LEAST

Q4 2028*

***Excludes** all near-term potential milestones from JNJ and Takeda

- **\$155M** in near-term - Icotrunkra
- **\$25M** Rusfertide
- **\$50M** (or \$75M if opted-out) Rusfertide NDA approval; and
- **Up to \$400M**, if we exercise opt-out option

SHARES
OUTSTANDING

~62.1M

as of
June 30, 2025



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 four Phase 3 psoriasis studies**
 - Psoriasis NDA submitted July 2025; EMA application submitted Sept 2025
- **Successful outcome in Phase 2b ulcerative colitis study**
 - Phase 3 in UC¹ initiated; Phase 2b/3 in Crohn's disease initiated²
- Potential annual peak sales of Icotrokinra: **\$5B+**^{3,4}
 - Tremfya® annual peak sales projected at \$10B+⁵
 - Skyrizi® annual peak sales projected at \$20B+ by 2027⁶
 - Psoriasis, psoriatic arthritis, ulcerative colitis, Crohn's disease

Approved Injectable
IL-23 Antagonist mAbs

Stelara®

Skyrizi®

Tremfya®

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

Icotrokinra Clinical Development Program

Successful Studies in Psoriasis & UC; PsA studies Ongoing; Phase 3 UC and CD studies underway

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

• Ongoing

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

• Ongoing

Psoriatic Arthritis

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

• Ongoing

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

• Ongoing

Ulcerative Colitis

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



ICONIC-UC Ph3, n~882, in ulcerative colitis

• New Study; recruiting

Crohn's Disease

ICONIC-CD Ph 2/3, n~1092, in Crohn's disease

• New Study; recruiting

Psoriasis
NDA submitted
July 2025

2025 EADV Meeting (17-20 September; Paris, France)

Icotrokinra Updates:

- ICONIC-ADVANCE 1 & 2
- ICONIC-LEAD



Icotrokinra Psoriasis Clinical Studies Update: EADV'25 Meeting

- **Phase 3 ICONIC-ADVANCE 1 & 2 studies¹** (Link to presentation [here](#))
 - **Icotrokinra met both co-primary endpoints compared to placebo at Week 16 with similar adverse event rates and showed superiority to deucravacitinib at multiple timepoints in adult patients**
 - Icotrokinra showed superior skin clearance vs placebo (Week 16) and deucravacitinib (Weeks 16 and 24)
 - Icotrokinra demonstrated similar adverse event rates (AEs) to placebo, with no new safety signals identified
 - Icotrokinra AE rates were numerically lower vs deucravacitinib through Week 24
- **Phase 3 ICONIC-LEAD study²** (Link to presentation [here](#))
 - **Icotrokinra demonstrated sustained skin clearance and a favorable safety profile through Week 52 with no new safety signals identified in the ICONIC-LEAD drug withdrawal/re-treatment study**
 - At Week 52, adult icotrokinra PASI 90 responders re-randomized to icotrokinra at Week 24 had superior maintenance of PASI 90 response versus those re-randomized to placebo (84% vs 21%; $p < 0.001$)
 - At Week 52, 86% of adolescents who received icotrokinra for the full 52 weeks and 77% of those who switched from placebo to icotrokinra at Week 16 achieved PASI 90 response
 - ICONIC-LEAD Week 16 primary endpoint data previously presented at the American Academy of Dermatology 2025 Congress³

1. Stein Gold, L et al. Icotrokinra Demonstrated Superior Responses Compared with Placebo and Deucravacitinib in the Treatment of Moderate-to-Severe Plaque Psoriasis : Results Through Week 24 of the Phase 3 ICONIC-ADVANCE 1 & 2 Studies. Oral presentation (Presentation FC01.1G) at the European Academy of Dermatology and Venereology Congress (EADV). September 2025.

2. Soung, J et al. Maintenance of Response with Icotrokinra, a Targeted Oral Peptide, for the Treatment of Moderate-to-Severe Psoriasis : Randomized Treatment Withdrawal in Adults (weeks 24-52) and Continuous Treatment in Adolescents (Through Week 52) From the Phase 3, ICONIC-LEAD Trial. Late-breaking research oral presentation (Presentation #D1T01.2B) at the European Academy of Dermatology and Venereology Congress (EADV). September 2025.

3. Bissonnette, R et al. Icotrokinra, a Targeted Oral Peptide That Selectively Blocks the Interleukin-23–Receptor, for the Treatment of Moderate-to-Severe Plaque Psoriasis: Results Through Week 24 of the Phase 3, Randomized, Double-blind, Placebo-Controlled ICONIC-LEAD Trial. Late-breaking research presentation (Abstract #66708) at the American Academy of Dermatology (AAD) 2024 Annual Meeting. March 2025.

ICONIC-ADVANCE 1 & 2: Key Takeaways

2025 EADV Meeting (17-20 September; Paris, France)

- In both of the pivotal Phase 3 ICONIC-ADVANCE 1 & 2 studies, adults with moderate-to-severe plaque PsO receiving icotrokinra (ICO) consistently demonstrated superior skin clearance and symptom relief vs PBO and Deucra:
- **ICO demonstrated significantly higher rates vs Deucra:**
 - Clear/almost clear skin
 - Completely clear skin (*~2-fold or greater*)
 - Symptom resolution
- **Favorable ICO safety:**
 - AE profile similar to PBO
 - Overall AE & infection rates lower than Deucra
 - No safety signal

ICO, a targeted oral peptide that binds and inhibits the IL-23R, has the potential to provide high rates of skin clearance and PsO symptom relief with a favorable safety profile in a once-daily pill

ICONIC-LEAD: Key Takeaways

2025 EADV Meeting (17-20 September; Paris, France)

- In the pivotal phase 3 ICONIC-LEAD study evaluating the targeted oral peptide icotrokinra (ICO) through 1 year in adults & adolescents with moderate-to-severe plaque PsO:

Continuous ICO demonstrated superior maintenance of skin response among **adult** W24 ICO responders:

- *89% and 84% maintained PASI 75 and PASI 90, respectively, at W52*
- *LOR vs ICO withdrawal: Not reached vs 17 weeks (PASI 75) or 10 weeks (PASI 90)*

Continuous ICO demonstrated robust and durable skin clearance rates in **adolescents** through W52:

- *PASI 90: 86%*
- *PASI 75: 95%*
- *IGA 0/1: 82%*

- ICO AE profile through W52 was consistent with that observed through W16

- No ICO safety signal was identified through W52



**Icotrokinra, a Targeted Oral Peptide that
Selectively Blocks IL-23 Receptor Activation,
in Moderately to Severely Active Ulcerative
Colitis: Week 12 Results from the Phase 2b,
Randomized, Double-blind, Placebo-
controlled, Treat-through, Dose-ranging
ANTHEM-UC Trial**

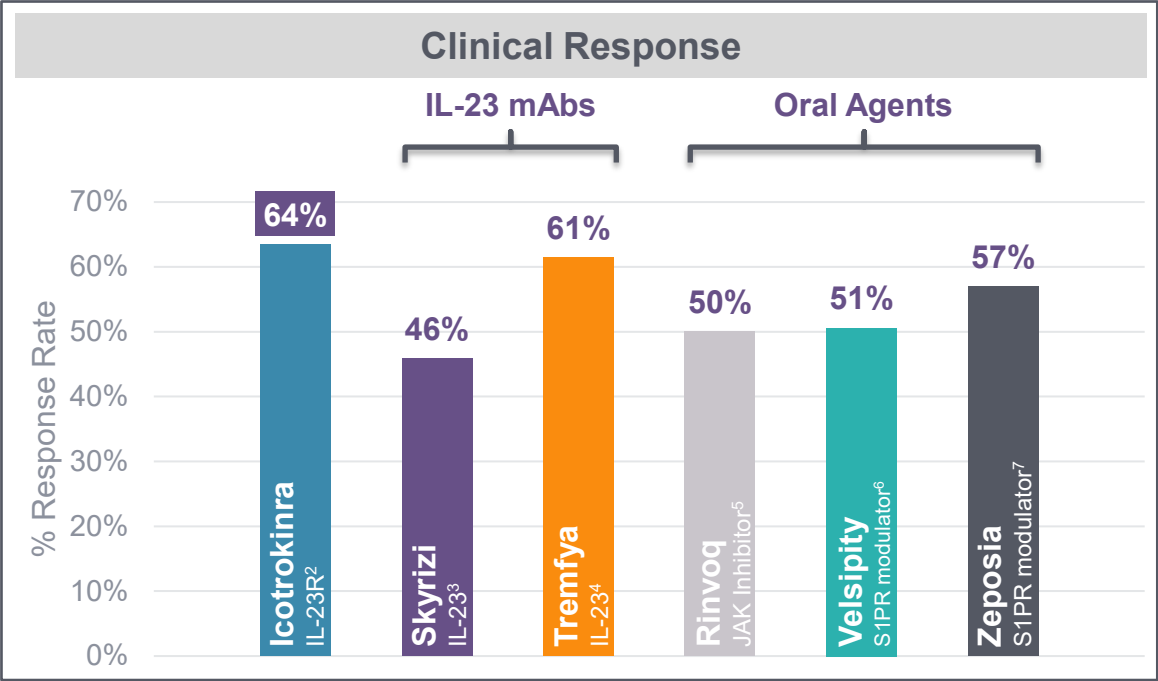
**UEGW 2025, Berlin, Germany & Online,
October 4-7, 2025**

Background and Objective

- Despite the availability of monoclonal antibodies and other agents targeting key inflammatory mediators, many patients with ulcerative colitis have inadequately controlled disease or do not tolerate available treatments
 - Ictrokinra has the potential to offer patients with moderately to severely active ulcerative colitis the standout combination of high efficacy and favorable safety profile with the simplicity of a once-daily oral pill
 - Ictrokinra (formerly JNJ-2113) is a first-in-class investigational targeted oral peptide that potently and selectively blocks the IL-23 receptor at the site of inflammation
- ANTHEM-UC (NCT06049017) evaluated the efficacy and safety of three doses of once-daily oral ictrokinra in adult participants with moderately to severely active ulcerative colitis

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.

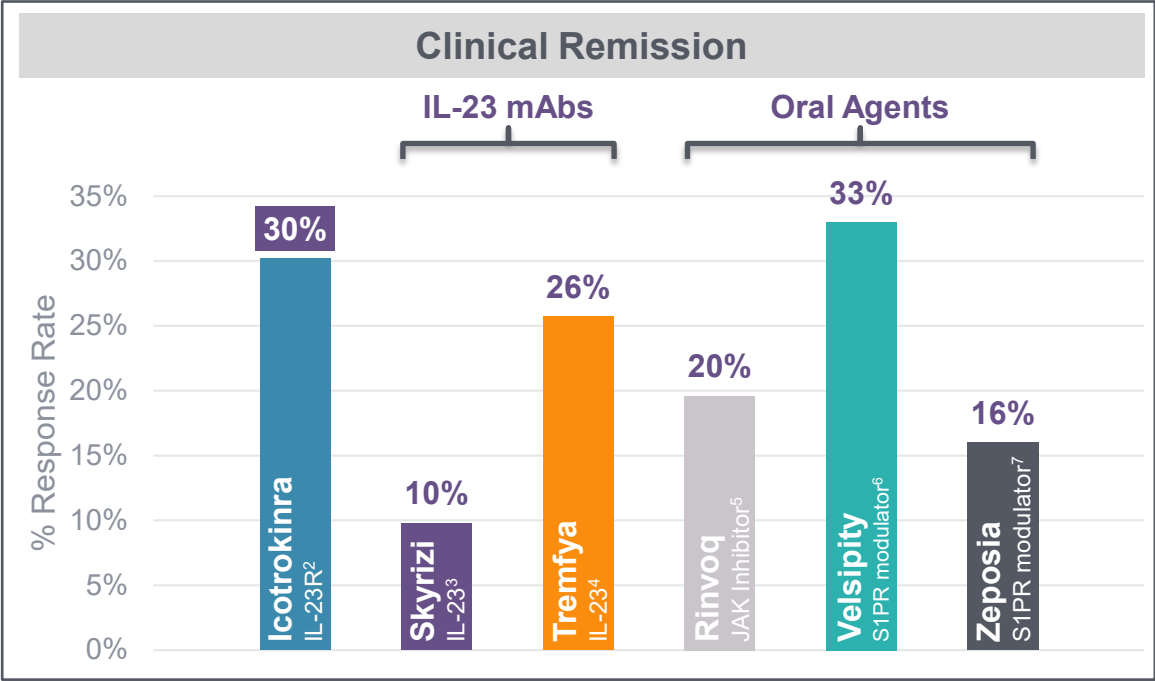
5. Rinvoq 45 mg PO QD (approved dose; phase 2 data) with clinical response at Wk 8 (ie, adapted Mayo score; defined as a decrease from baseline in the adapted Mayo score of 2 points and 30% from baseline, plus a decrease in rectal bleeding score of 1 or an absolute rectal bleeding score of 1). Clinical 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.

ANTHEM-UC Study Design

Key Eligibility Criteria

- Diagnosed UC of ≥12 weeks duration and a Modified Mayo score (mMS) of 5–9, inclusive
- Mayo endoscopy subscore (MES) ≥2 per central review of screening video endoscopy
- Inadequate response/intolerance (IR) to corticosteroids, 6-MP, or AZA OR corticosteroid dependence OR IR to TNF α antagonists, ustekinumab, vedolizumab, JAK inhibitors, or S1P modulators (BIO/JAKi /S1Pm-IR)



★ **Primary Endpoint (Clinical Response at W12)**



Stratification

- BIO/JAKi /S1Pm-IR status: Yes or No
- Baseline MES: 2 or 3

Testing Procedure and Statistical Considerations

- **Primary Endpoint**
 - Clinical response vs placebo at Week 12
- **Secondary Endpoints (all vs placebo at Week 12)**
 - Clinical remission
 - Symptomatic remission
 - Endoscopic improvement
 - Histologic-endoscopic mucosal improvement (HEMI)
- ☑ Study powered to detect a treatment difference between icotrokinra 400 mg and placebo for the primary endpoint; it was not powered for the secondary endpoints
- ☑ Statistical testing was conducted sequentially: if a comparison was $p \geq 0.05$, all subsequent comparisons were not significant and nominal p-values are presented

Demographics and Baseline Disease Characteristics



	Placebo	Icotrokinra 100 mg QD	Icotrokinra 200 mg QD	Icotrokinra 400 mg QD	Total
Full analysis set, n	63	64	62	63	252
Age, years, mean (SD)	38.3 (13.8)	45.8 (14.6)	41.8 (14.6)	40.6 (14.8)	41.6 (14.7)
Sex, male, n (%)	35 (55.6%)	40 (62.5%)	32 (51.6%)	40 (63.5%)	147 (58.3%)
Race, White, n (%)	44 (69.8%)	45 (70.3%)	39 (62.9%)	42 (66.7%)	170 (67.5%)
UC disease duration, years, mean (SD)	8.3 (8.1)	7.4 (6.1)	7.8 (7.5)	7.6 (7.6)	7.8 (7.3)
Extensive disease, n (%)	27 (42.9%)	23 (35.9%)	23 (37.1%)	29 (46.0%)	102 (40.5%)
Modified Mayo score [max = 9], mean (SD)	6.75 (1.231)	6.55 (1.296)	6.75 (1.386)	6.49 (1.401)	6.63 (1.327)
Mayo endoscopic subscore of 3 (severe), n (%)	36 (57.1%)	38 (59.4%)	37 (59.7%)	37 (58.7%)	148 (58.7%)
Fecal calprotectin, mg/kg, median [IQR]	1467.0 [420.5; 3622.0]	1433.3 [698.0; 3121.2]	2467.0 [646.4; 4599.6]	1421.3 [584.6; 4978.6]	1523.0 [587.0; 3816.7]
CRP, mg/L, median [IQR]	3.0 [0.9; 7.0]	3.0 [1.1; 6.7]	5.3 [1.5; 11.3]	4.0 [1.5; 8.1]	3.6 [1.3; 8.1]

Demographics and Baseline Disease Characteristics (Continued)



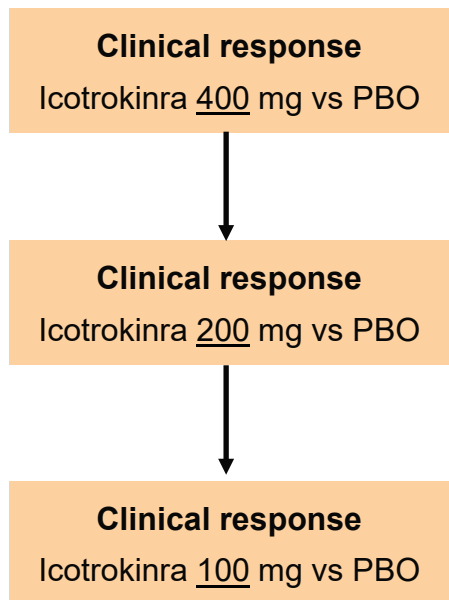
	Placebo	Icotrokinra 100 mg QD	Icotrokinra 200 mg QD	Icotrokinra 400 mg QD	Total
Full analysis set, n	63	64	62	63	252
Baseline corticosteroid use, n (%)	21 (33.3%)	21 (32.8%)	29 (46.8%)	23 (36.5%)	94 (37.3%)
Baseline immunomodulator use, n (%)	16 (25.4%)	10 (15.6%)	10 (16.1%)	6 (9.5%)	42 (16.7%)
No history of BIO/JAKi/S1Pm-IR, n (%)	35 (55.6%)	38 (59.4%)	36 (58.1%)	34 (54.0%)	143 (56.7%)
History of BIO/JAKi/S1Pm-IR, n (%)	28 (44.4%)	26 (40.6%)	26 (41.9%)	29 (46.0%)	109 (43.3%)
IR to 1 class / mechanism ^a	22 (78.6%)	19 (73.1%)	21 (80.8%)	15 (51.7%)	77 (70.6%)
IR to 2 classes / mechanisms ^a	6 (21.4%)	6 (23.1%)	5 (19.2%)	14 (48.3%)	31 (28.4%)
IR to >2 classes / mechanisms ^a	0	1 (3.8%)	0	0	1 (0.9%)

Multiple Testing Procedure and Statistical Considerations



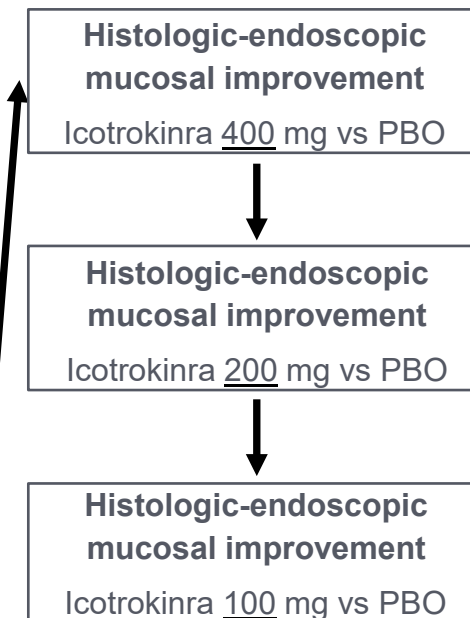
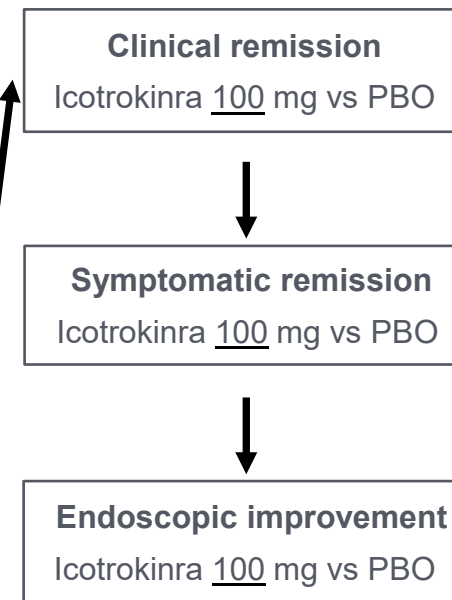
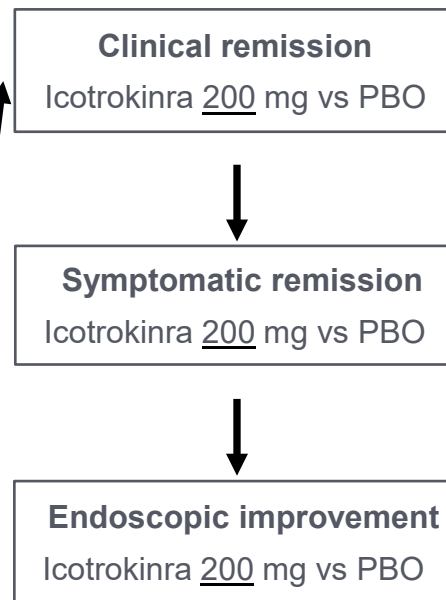
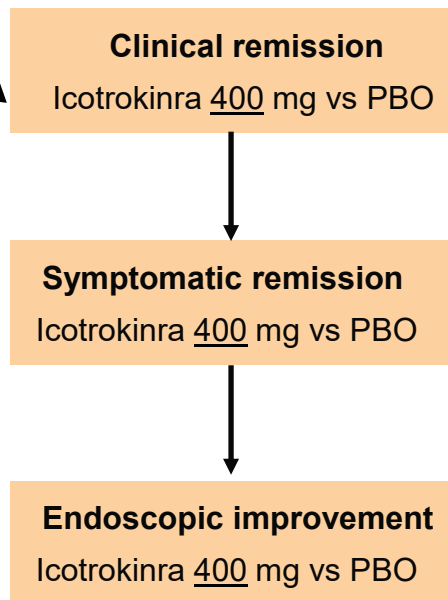
Primary endpoints

(Week 12)



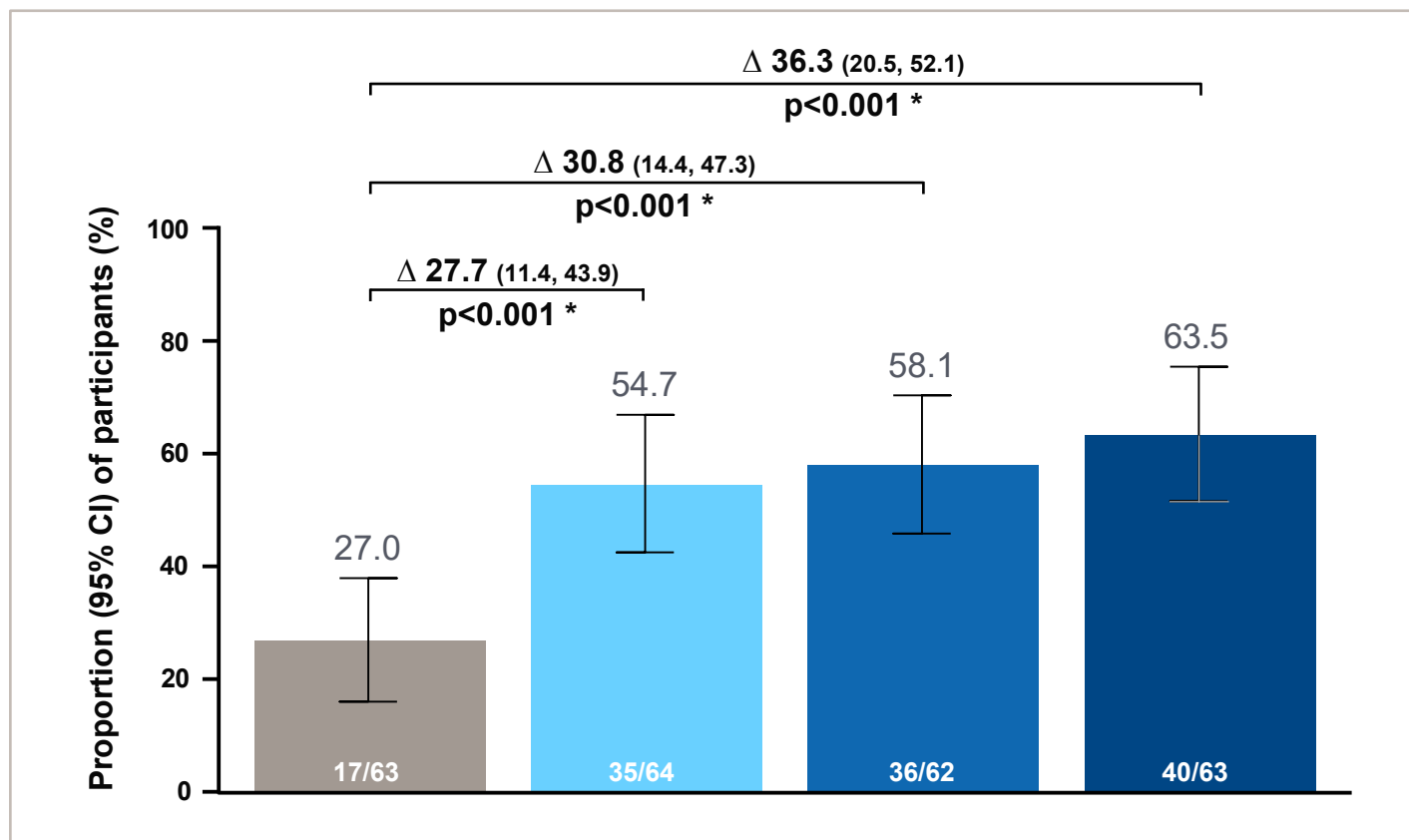
Secondary endpoints

(Week 12)



- ✓ Statistical testing was conducted sequentially: if a comparison was $p \geq 0.05$, all subsequent comparisons were not significant, and nominal p-values are presented
- ✓ The study was powered to detect a treatment difference between icotrokinra 400 mg and placebo for the primary endpoint; it was not powered for the secondary endpoints

Primary Endpoint: Clinical Response at Week 12



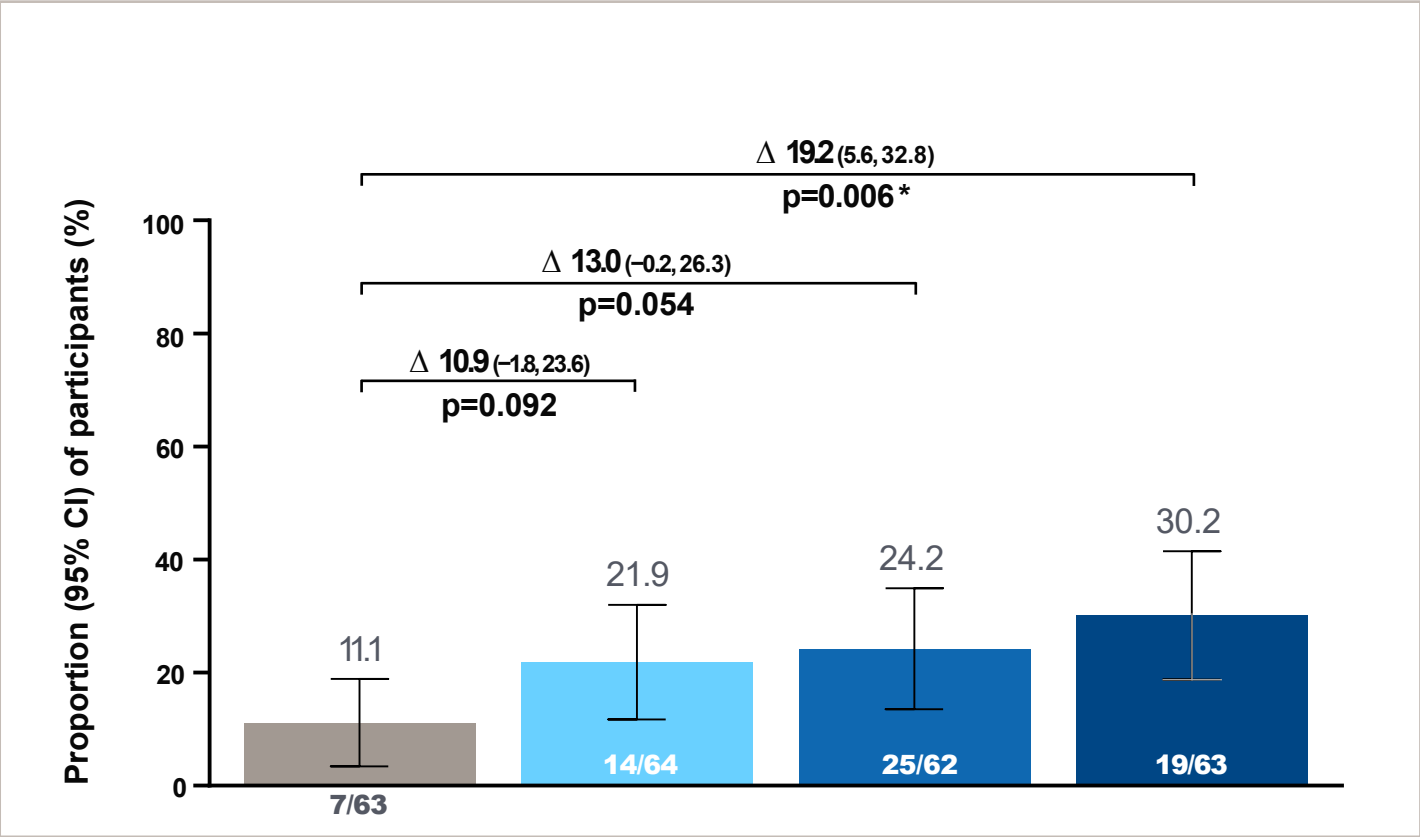
- Placebo
- Icotrokinra 100 mg qd
- Icotrokinra 200 mg qd
- Icotrokinra 400 mg qd

*Statistically significant based on testing procedure

Clinical response: a decrease from baseline in the modified Mayo score by $\geq 30\%$ 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

Δ = adjusted treatment difference (95% confidence interval) and p-value vs placebo. Adjusted treatment differences, 95% CIs, and p-values were based on the common risk difference by use of Mantel-Haenszel stratum weights and the Sato variance estimator, using stratification factors of BIO/JAKi/S1Pm-IR status (Yes or No) and Mayo endoscopy subscore (moderate [2] or severe [3]). Participants with intercurrent events of ostomy or colectomy, prohibited changes in UC medication, or discontinuation of study intervention for any reason except those due to major disruptions (e.g., COVID-19 related reasons or regional crisis, excluding COVID-19 infection) were considered nonresponders, as were participants who had missing data for the endpoint. For participants discontinuing study intervention due to major disruptions, their observed values, if available, were used. After accounting for these scenarios, participants who were missing data necessary for calculation of the outcome measure at the assessment timepoint were considered not to have achieved that endpoint.

Clinical Remission at Week 12



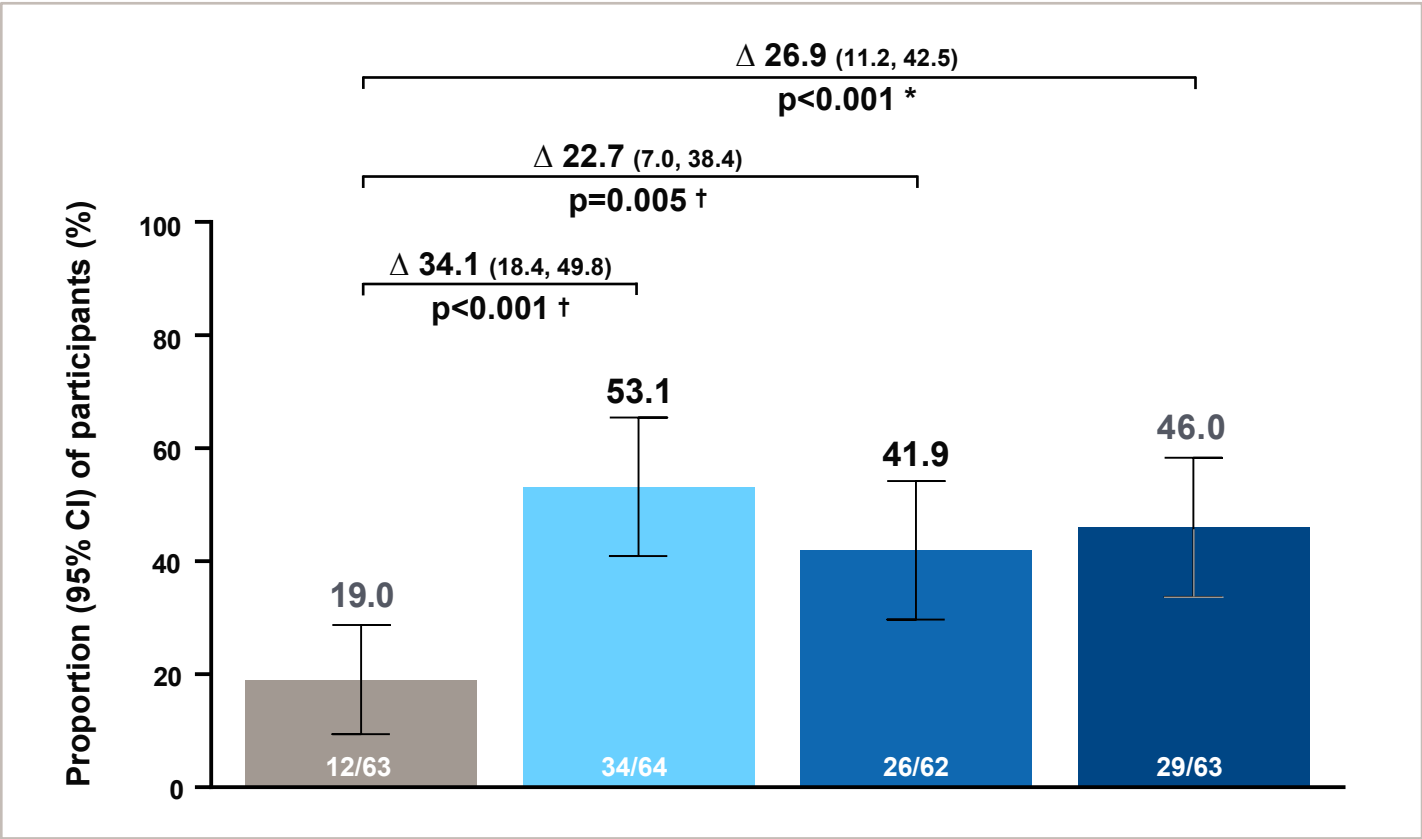
- Placebo
- Icotrokinra 100 mg qd
- Icotrokinra 200 mg qd
- Icotrokinra 400 mg qd

*Statistically significant based on testing procedure

Clinical remission: stool frequency subscore of 0 or 1, rectal bleeding subscore of 0, and Mayo endoscopy subscore of 0 or 1

Δ = adjusted treatment difference (95% confidence interval) and p-value vs placebo. Adjusted treatment differences, 95% CIs, and p-values were based on the common risk difference by use of Mantel-Haenszel stratum weights and the Sato variance estimator, using stratification factors of BIO/JAKi/S1Pm-IR status (Yes or No) and Mayo endoscopy subscore (moderate [2] or severe [3]). Participants with intercurrent events of ostomy or colectomy, prohibited changes in UC medication, or discontinuation of study intervention for any reason except those due to major disruptions (e.g., COVID-19 related reasons or regional crisis, excluding COVID-19 infection) were considered nonresponders, as were participants who had missing data for the endpoint. For participants discontinuing study intervention due to major disruptions, their observed values, if available, were used. After accounting for these scenarios, participants who were missing data necessary for calculation of the outcome measure at the assessment timepoint were considered not to have achieved that endpoint.

Symptomatic Remission at Week 12



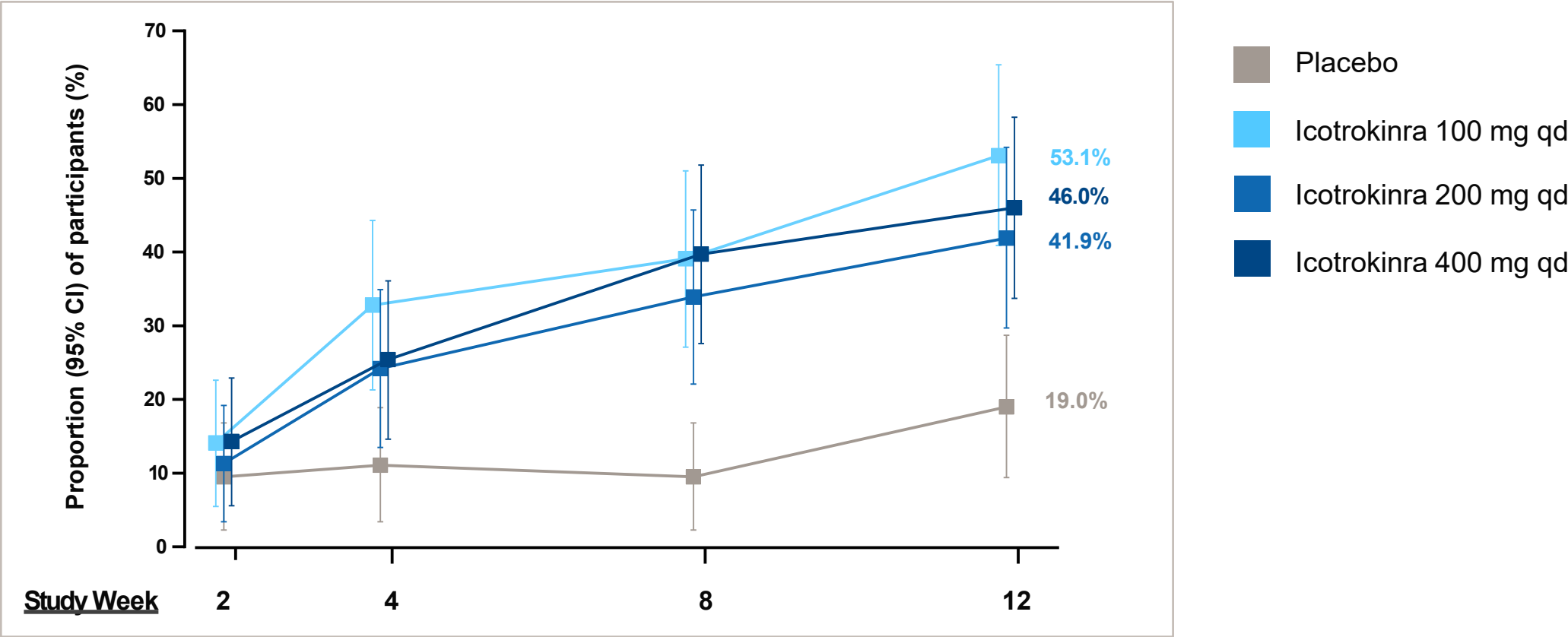
- Placebo
- Icotrokinra 100 mg qd
- Icotrokinra 200 mg qd
- Icotrokinra 400 mg qd

* Statistically significant based on testing procedure
† Nominal p-value <0.05

Symptomatic remission: stool frequency subscore of 0 or 1 and rectal bleeding subscore of 0

Δ = adjusted treatment difference (95% confidence interval) and p-value vs placebo. Adjusted treatment differences, 95% CIs, and p-values were based on the common risk difference by use of Mantel-Haenszel stratum weights and the Sato variance estimator, using stratification factors of BIO/JAKi/S1Pm-IR status (Yes or No) and Mayo endoscopy subscore (moderate [2] or severe [3]). Participants with intercurrent events of ostomy or colectomy, prohibited changes in UC medication, or discontinuation of study intervention for any reason except those due to major disruptions (e.g., COVID-19 related reasons or regional crisis, excluding COVID-19 infection) were considered nonresponders, as were participants who had missing data for the endpoint. For participants discontinuing study intervention due to major disruptions, their observed values, if available, were used. After accounting for these scenarios, participants who were missing data necessary for calculation of the outcome measure at the assessment timepoint were considered not to have achieved that endpoint.

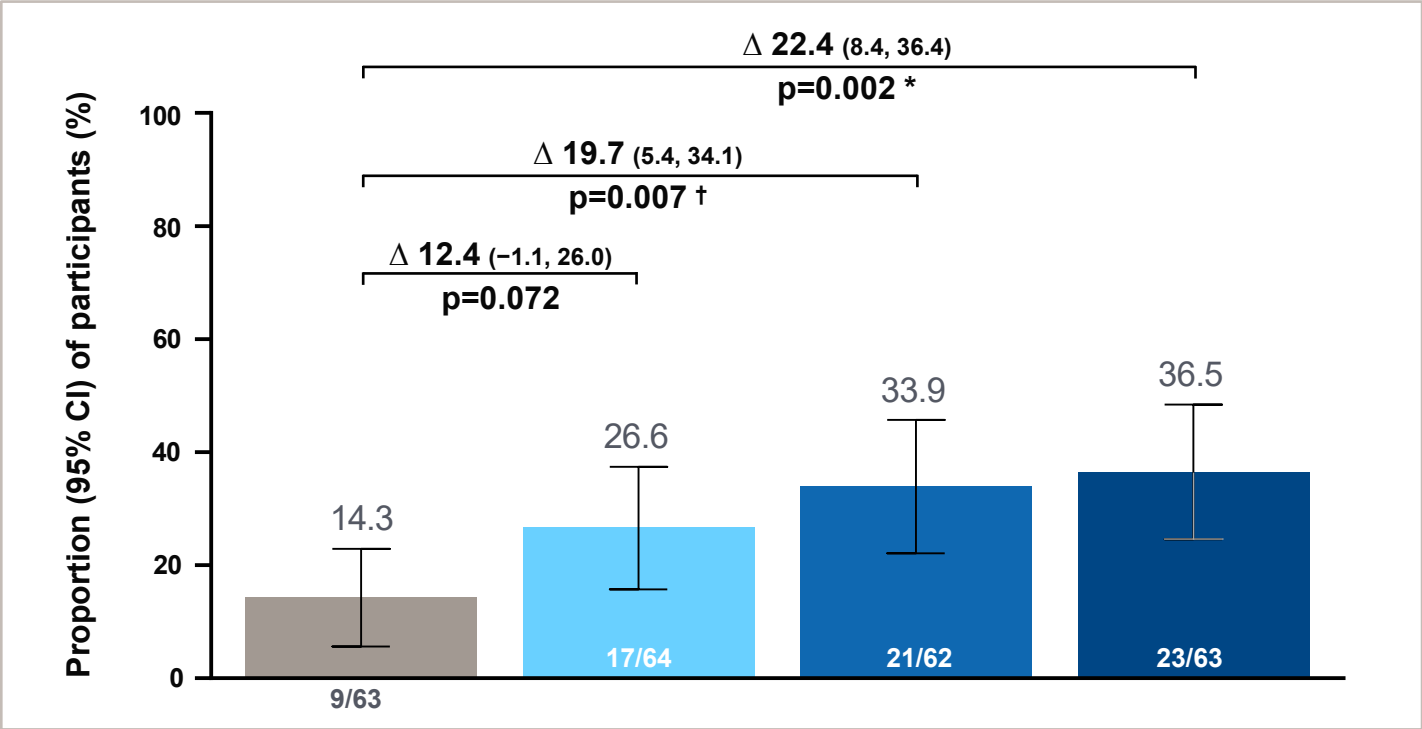
Symptomatic Remission Through Week 12



Symptomatic remission: stool frequency subscore of 0 or 1 and rectal bleeding subscore of 0

Δ = adjusted treatment difference (95% confidence interval) and p-value vs placebo. Adjusted treatment differences, 95% CIs, and p-values were based on the common risk difference by use of Mantel-Haenszel stratum weights and the Sato variance estimator, using stratification factors of BIO/JAKi/S1Pm-IR status (Yes or No) and Mayo endoscopy subscore (moderate [2] or severe [3]). Participants with intercurrent events of ostomy or colectomy, prohibited changes in UC medication, or discontinuation of study intervention for any reason except those due to major disruptions (e.g., COVID-19 related reasons or regional crisis, excluding COVID-19 infection) were considered nonresponders, as were participants who had missing data for the endpoint. For participants discontinuing study intervention due to major disruptions, their observed values, if available, were used. After accounting for these scenarios, participants who were missing data necessary for calculation of the outcome measure at the assessment timepoint were considered not to have achieved that endpoint.

Endoscopic Improvement at Week 12



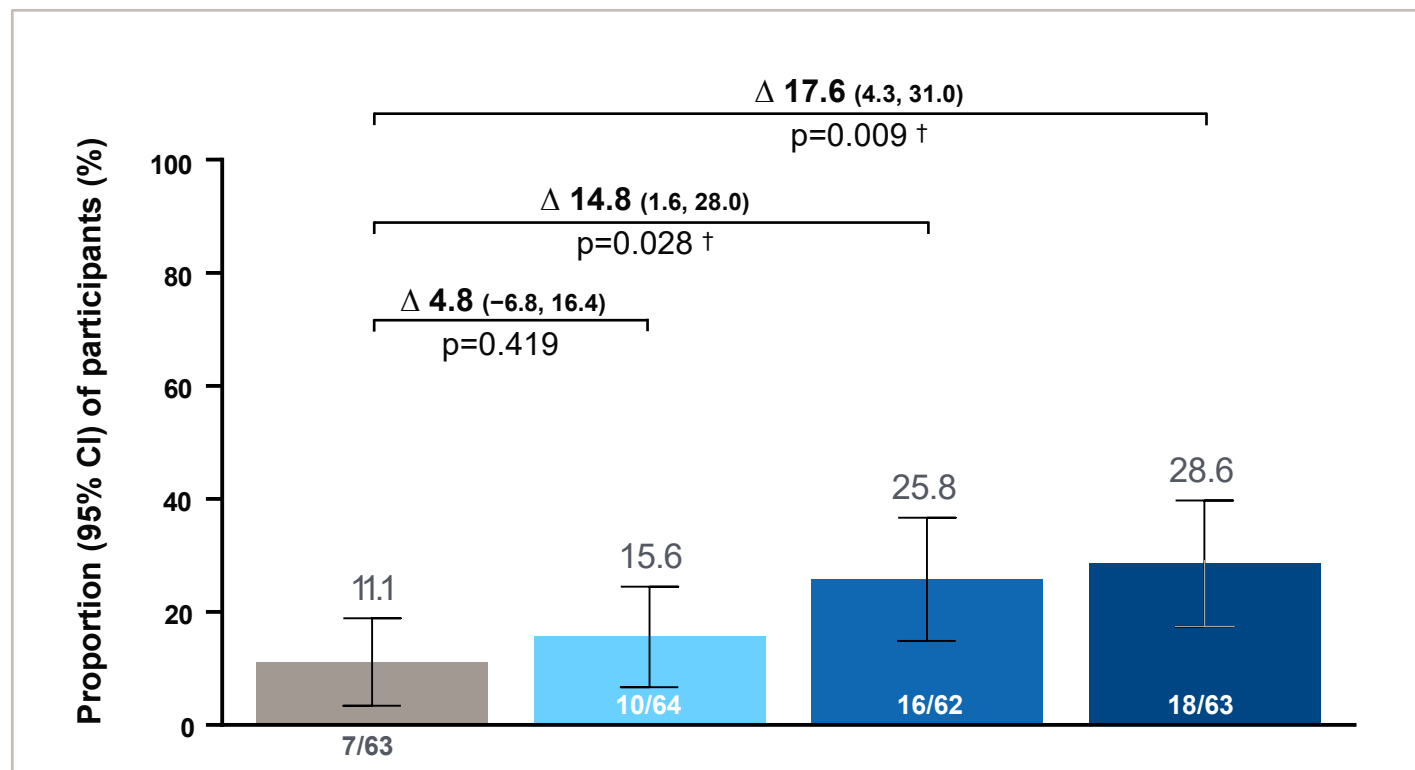
- Placebo
- Icotrokinra 100 mg qd
- Icotrokinra 200 mg qd
- Icotrokinra 400 mg qd

* Statistically significant based on testing procedure
† Nominal p-value <0.05

Endoscopic improvement: Mayo endoscopy subscore of 0 or 1

Δ = adjusted treatment difference (95% confidence interval) and p-value vs placebo. Adjusted treatment differences, 95% CIs, and p-values were based on the common risk difference by use of Mantel-Haenszel stratum weights and the Sato variance estimator, using stratification factors of BIO/JAKi/S1Pm-IR status (Yes or No) and Mayo endoscopy subscore (moderate [2] or severe [3]). Participants with intercurrent events of ostomy or colectomy, prohibited changes in UC medication, or discontinuation of study intervention for any reason except those due to major disruptions (e.g., COVID-19 related reasons or regional crisis, excluding COVID-19 infection) were considered nonresponders, as were participants who had missing data for the endpoint. For participants discontinuing study intervention due to major disruptions, their observed values, if available, were used. After accounting for these scenarios, participants who were missing data necessary for calculation of the outcome measure at the assessment timepoint were considered not to have achieved that endpoint.

Histologic–Endoscopic Mucosal Improvement (HEMI) at Week 12



- Placebo
- Icotrokinra 100 mg qd
- Icotrokinra 200 mg qd
- Icotrokinra 400 mg qd

† Nominal p-value <0.05

Histologic-endoscopic mucosal improvement: histologic remission (absence of neutrophils from the mucosa in both lamina propria and epithelium, no crypt destruction, and no erosions, ulcerations, or granulation tissue according to the Geboes grading system) AND endoscopic improvement (MES of 0 or 1)

Δ = adjusted treatment difference (95% confidence interval) and p-value vs placebo. Adjusted treatment differences, 95% CIs, and p-values were based on the common risk difference by use of Mantel-Haenszel stratum weights and the Sato variance estimator, using stratification factors of BIO/JAK1/S1Pm-IR status (Yes or No) and Mayo endoscopy subscore (moderate [2] or severe [3]). Participants with intercurrent events of ostomy or colectomy, prohibited changes in UC medication, or discontinuation of study intervention for any reason except those due to major disruptions (e.g., COVID-19 related reasons or regional crisis, excluding COVID-19 infection) were considered nonresponders, as were participants who had missing data for the endpoint. For participants discontinuing study intervention due to major disruptions, their observed values, if available, were used. After accounting for these scenarios, participants who were missing data necessary for calculation of the outcome measure at the assessment timepoint were considered not to have achieved that endpoint.

Summary of Adverse Events Through Week 12

	Placebo	Icotrokinra 100 mg QD	Icotrokinra 200 mg QD	Icotrokinra 400 mg QD
Safety analysis set, N	63	64	62	63
Average duration of follow-up, weeks	11.7	12.0	12.0	11.9
Average duration of treatment, weeks	11.2	11.8	11.7	11.6
Deaths, n (%)	0	0	0	0
Participants with 1 or more, n (%)				
AEs	32 (50.8%)	32 (50.0%)	28 (45.2%)	29 (46.0%)
Serious AEs	3 (4.8%)	0	2 (3.2%)	1 (1.6%)
AEs leading to discontinuation of study agent	5 (7.9%)	0	4 (6.5%)	1 (1.6%)
Infections ^a	12 (19.0%)	11 (17.2%)	16 (25.8%)	12 (19.0%)
Serious infections ^a	1 (1.6%)	0	0	0
Most common AEs (frequency ≥5% in any group), n (%)				
Worsening of ulcerative colitis	5 (7.9%)	3 (4.7%)	5 (8.1%)	3 (4.8%)
Headache	1 (1.6%)	5 (7.8%)	2 (3.2%)	4 (6.3%)
Upper respiratory tract infection	1 (1.6%)	4 (6.3%)	3 (4.8%)	4 (6.3%)
Nasopharyngitis	1 (1.6%)	3 (4.7%)	0	6 (9.5%)
COVID-19	0	0	4 (6.5%)	0

Conclusions

- ✓ In adults with moderately to severely active ulcerative colitis, all tested doses of once-daily oral icotrokinra achieved the primary endpoint of clinical response at Week 12
- ✓ At Week 12, icotrokinra 400 mg QD was superior to placebo for clinical remission, symptomatic remission, and endoscopic improvement with clinically meaningful differences observed for histologic–endoscopic mucosal improvement (HEMI)
- ✓ Icotrokinra was well tolerated: the proportions of participants experiencing AEs through Week 12 were similar for placebo and all icotrokinra doses
- ✓ Icotrokinra, the first-in-class targeted oral peptide that selectively blocks the IL-23 receptor, has potential to offer therapeutic benefit with a favorable safety profile in a once-daily oral treatment for ulcerative colitis

Icotrokinra Phase 2 ANTHEM-UC Study¹

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.

Next Steps:

Icotrokinra Phase 3 Ulcerative Colitis and Phase 2b/3 Crohn's Disease Clinical Studies Update

- Phase 3 ICONIC-UC study in adult and adolescent participants with moderately to severely active ulcerative colitis¹:
 - Double-blind induction study (primary endpoint at Week 12):
 - Percentage of adult participants in clinical remission^a
 - Double-blind maintenance study (primary endpoint at Week 40):
 - Percentage of adult participants in clinical remission^a
 - Open-label maintenance phase (primary endpoint at Week 40):
 - Percentage of adolescent participants in clinical remission^a
- Phase 2/3 ICONIC-CD study in participants with moderately to severely active Crohn's disease²:
 - Induction study 1 (primary endpoint at Week 12):
 - Number of participants with clinical response^b
 - Induction study 2 (co-primary endpoints at Week 12):
 - Number of participants with clinical remission^c
 - Number of participants with endoscopic response^d
 - Maintenance study (co-primary endpoints at Week 40):
 - Number of participants with clinical remission^c
 - Number of participants with endoscopic response^d

Potential registration-enabling, phase 3 studies underway in participants with moderately to severely active ulcerative colitis and Crohn's disease

^aClinical remission is defined as stool frequency subscore of 0 or 1, a rectal bleeding subscore of 0, and an endoscopy subscore of 0 or 1.

^bClinical response is defined as ≥100-point reduction from baseline in Crohn's Disease Activity Index (CDAI) score. CDAI scores range from 0 to approximately 600. Higher score indicates higher disease activity.

^cClinical remission is defined as CDAI score <150. CDAI scores range from 0 to approximately 600. Higher score indicates higher disease activity.

^dEndoscopic response is defined as >50% improvement from baseline in Simple Endoscopic Score for Crohn's Disease (SES-CD) score or a decrease of at least 2 points in participants with a baseline score of 4 and isolated ileal disease. SES-CD score can range from 0 to 56. Higher scores indicate more severe disease.

Icotrokinra Summary

NDA Seeking FDA Approval for Plaque Psoriasis Submitted July 2025

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 underway

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

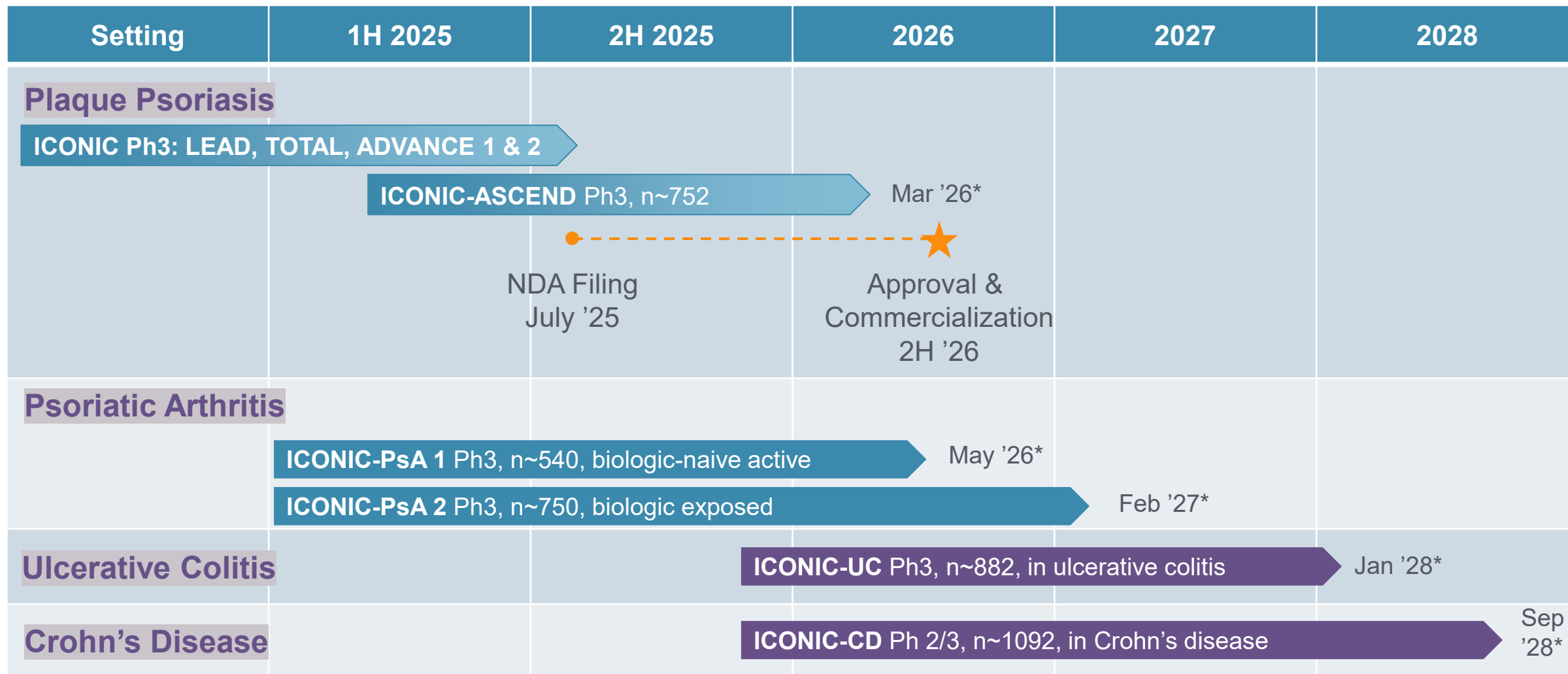
Ulcerative Colitis (UC)

- 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
- ICONIC-UC Phase 3 study initiated

Crohn's Disease (CD)

- ICONIC-CD phase 2/3 study initiated

Icotrokinra: Clinical Development, Approval and Commercialization Timelines



Rusfertide

A Synthetic Mimetic of the Natural Hormone Hepcidin

Addressing Unmet Needs in
Polycythemia Vera



Polycythemia Vera (PV)

Disease Background

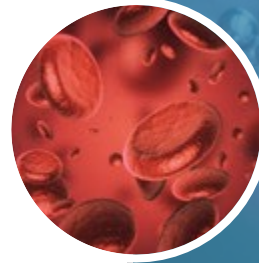
Rare myeloproliferative neoplasm characterized by excessive production of red blood cells (RBCs)¹

- 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 (PV)

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.

4. Griesshammer M, et al. *Ann Hematol*. 2019;98(5):1071-1082.

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.

6. Mesa R, et al. *BMC Cancer* 2016;16:167.

7. Ginzburg et al. *Leukemia* 2018;32:2105-2116.

Identifying PV Patients Who Will Benefit From Rusfertide

Defining patient population characteristics 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

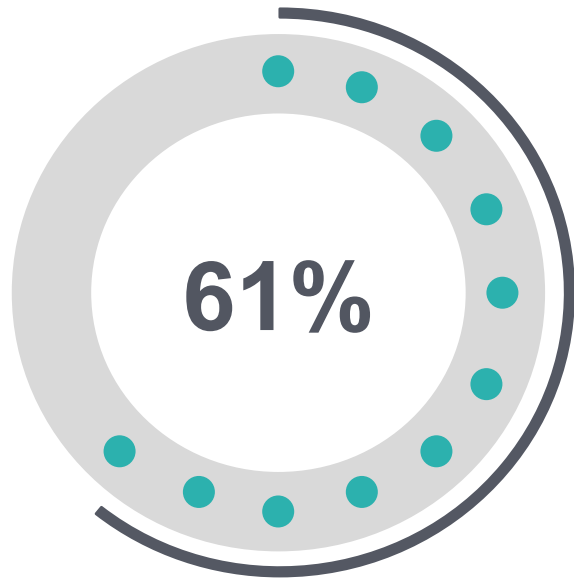
Thrombotic Events



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

Most Patients With Polycythemia Vera Experience Suboptimal Hct Control

Frequent Phlebotomies, High-Dose Hydroxyurea and/or Post-Treatment TEs Are Common



61%

**Regimens among patients with PV
who received burdensome treatment
and/or experienced a TE (N=27,116)¹**

54%



Frequent phlebotomies (PHLs)

Patients receiving ≥ 3 PHLs in 6 months

28%



High-dose hydroxyurea (HU)

Patients receiving $\geq 1,000$ mg HU per day

8%



Combination of PHL and HU

Patients receiving a combination of
frequent phlebotomies and high-dose HU

Rusfertide Launch Readiness



Market Insights

Generate key market insights to inform commercial strategy, data generation and payer evidence



Clinical Value

Rapid, consistent and durable Hct control + symptom relief, which fulfills a significant unmet need and benefits patients



Scientific Exchange

Data generation, medical communications, awareness of unmet need in PV, MSLs, advisory boards



Ensure Access

Market access strategy which navigates dynamic payer landscape and is aligned with clinical value and supported by clinical evidence

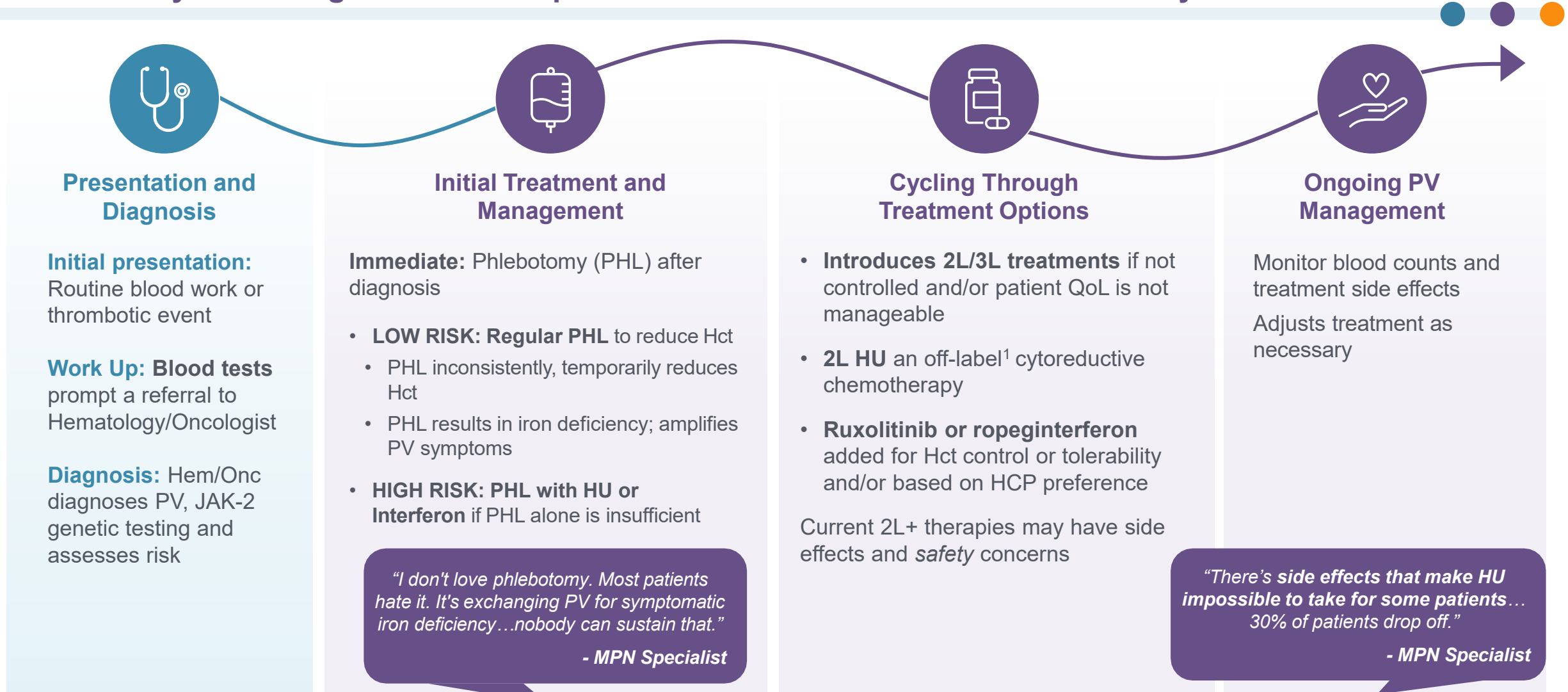


Scale For Success

Customer engagement model which supports patient needs and maximizes the opportunity for rusfertide

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 <i>Kremyanskaya, M, et al. New Engl J Med; 2024;390:723-35</i>
		THRIVE LTE, n=46				• Ongoing; for REVIVE patients in OLE
		PACIFIC Ph 2, Elevated Hct (>48%), n=20				• Completed

Rusfertide has **Orphan Drug** designation, **Fast Track** status, and **Breakthrough Therapy Designation** for PV

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

Rusfertide Phase 3 **VERIFY** Study

Clinical Study Design and Topline Results

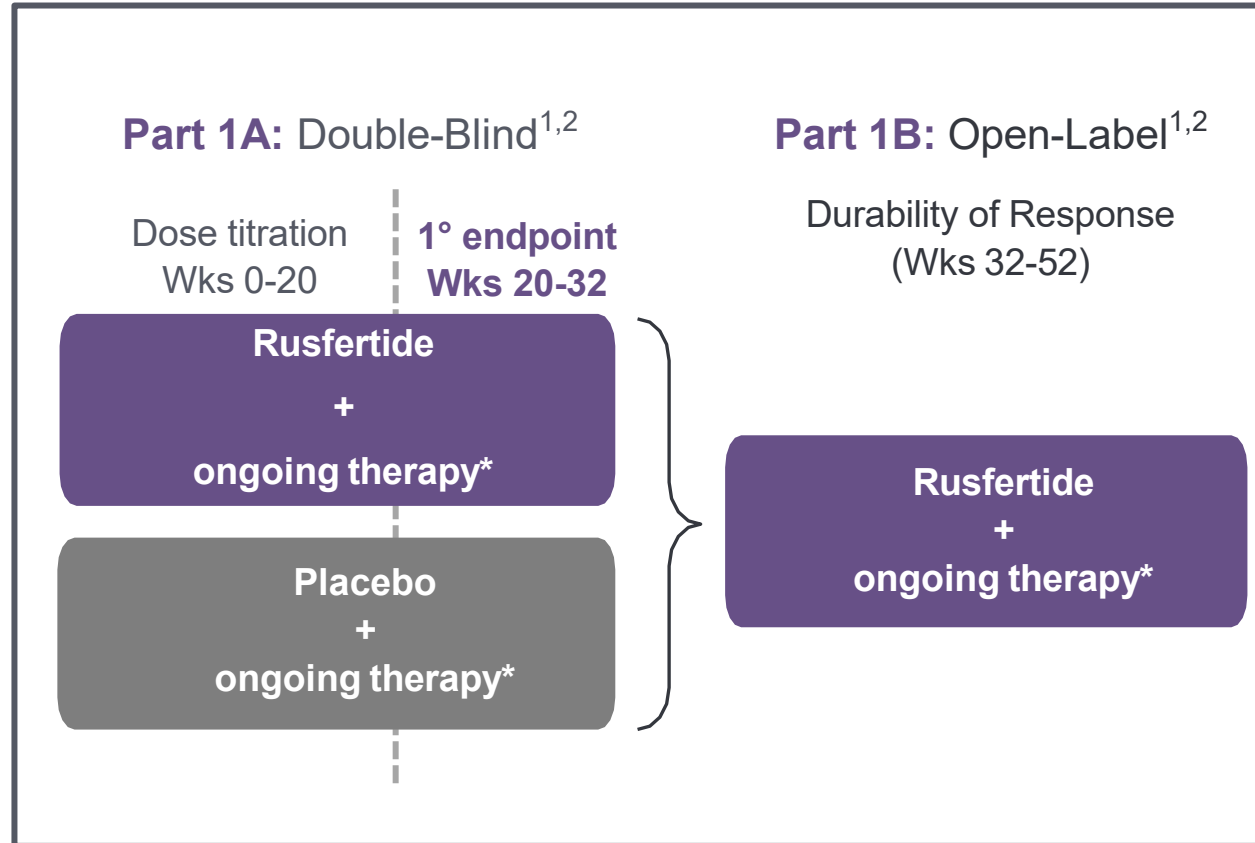
ASCO 2025
Plenary
Session

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

Key Takeaway Points from Phase 3 VERIFY Study in Polycythemia Vera (PV)¹

Link to Phase 3 VERIFY Study Results Presentation Available [Here](#)

VERIFY is a **global, randomized, double-blind phase 3 study** investigating rusfertide or placebo with current standard-of-care therapy in patients with PV

VERIFY met its prespecified primary endpoint (response) **and all four key secondary endpoints**, including reduction in phlebotomy and improvement in symptoms (assessed by PRO measures) vs. placebo

Rusfertide was well tolerated and had a safety profile that was consistent with prior observations in phase 2 studies of patients with PV, including REVIVE

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 presented in oral plenary presentation at ASCO'25⁹ and will be included in regulatory filings (eg, NDA, MAA)

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

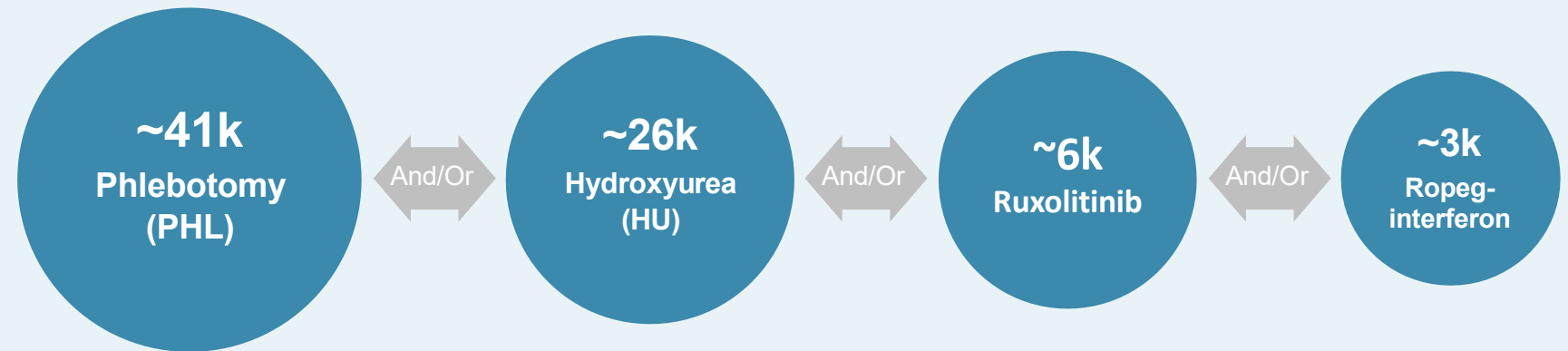
Polycythemia Vera: Prevalence, Treatment Paradigm and Unmet Need

Uncontrolled Hematocrit Exists at Each Step of Treatment

**~155k
diagnosed**
patients in the US with
~78k treated²

Treatment Paradigm

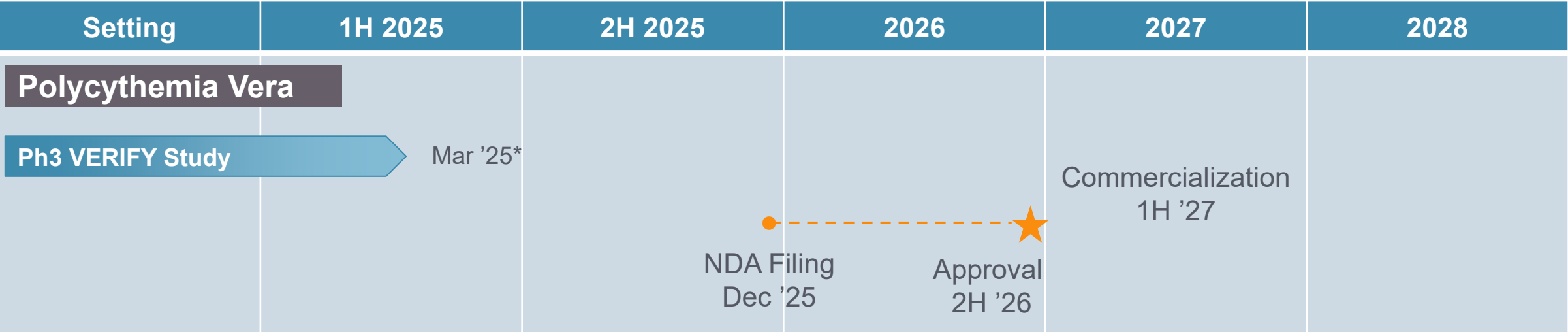
Patients are often on polytherapy and will cycle through various treatments²



- Unmet need exists at each step of the treatment landscape
 - ~78% with uncontrolled Hct<45%³
- Rusfertide expected to be used at each step¹

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

Rusfertide for PV: Clinical Development, Approval and Commercialization Timelines



* Primary Completion Date

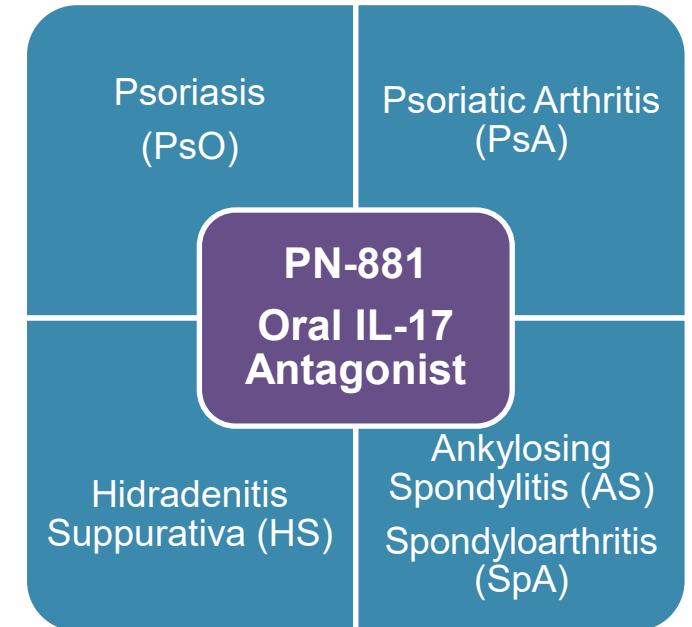
**PN-881:
Oral Peptide IL-17
Antagonist Development
Candidate**



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



1. Psoriasis Disease Landscape and Forecast (Clarivate, 2023);

2. No approved oral IL-17 antagonists. Approved IL-17 mAbs: COSENTYX (secukinumab), TALTZ (ixekizumab), and BIMZELX (bimekizumab)

3. Blockade of both IL-17A and IL-17F leads to greater efficacy. Reich et al., N Engl J Med 2021;385:142-52. DOI: 10.1056/NEJMoa2102383

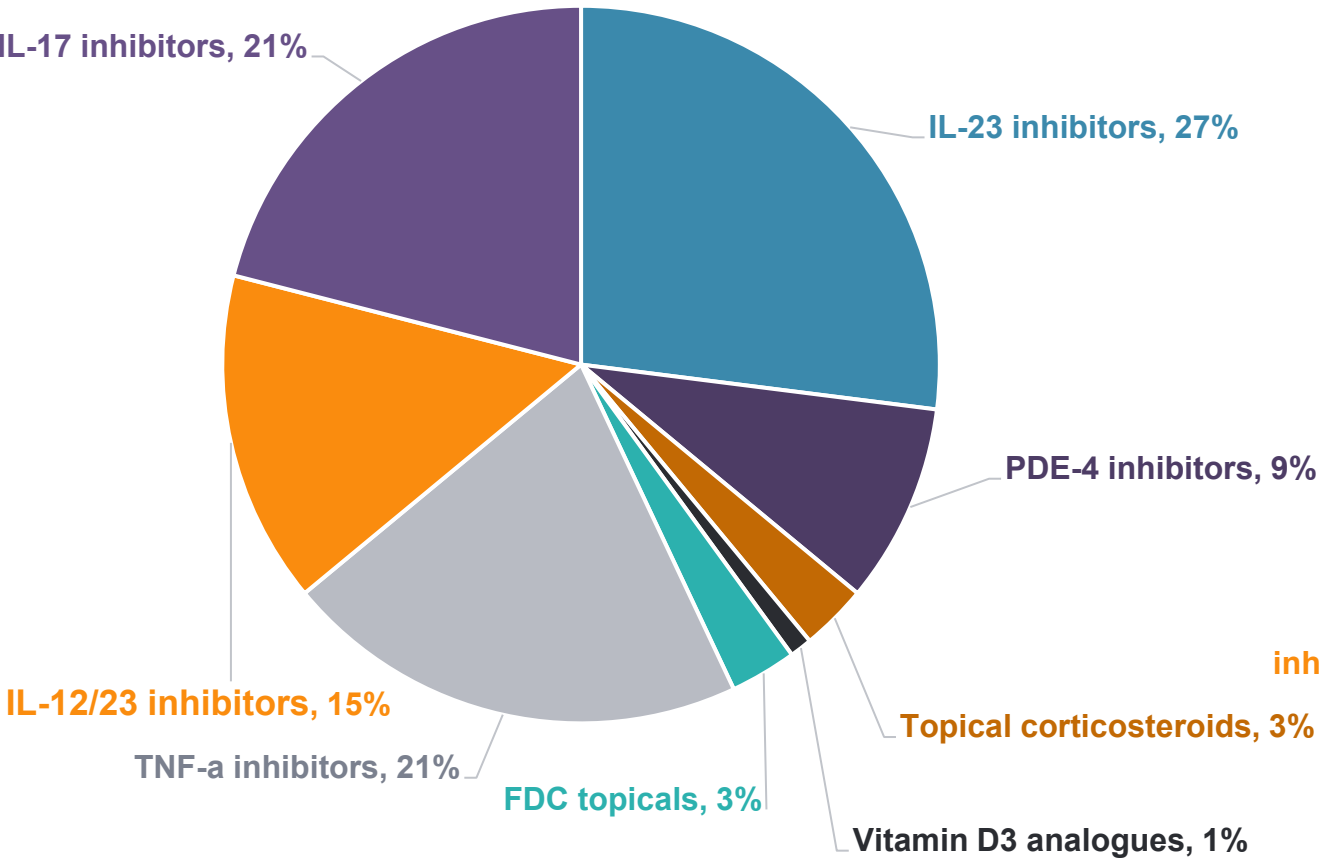
4. SAD = single ascending dose, MAD = multiple ascending dose

Psoriasis Market Share by Drug Class

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

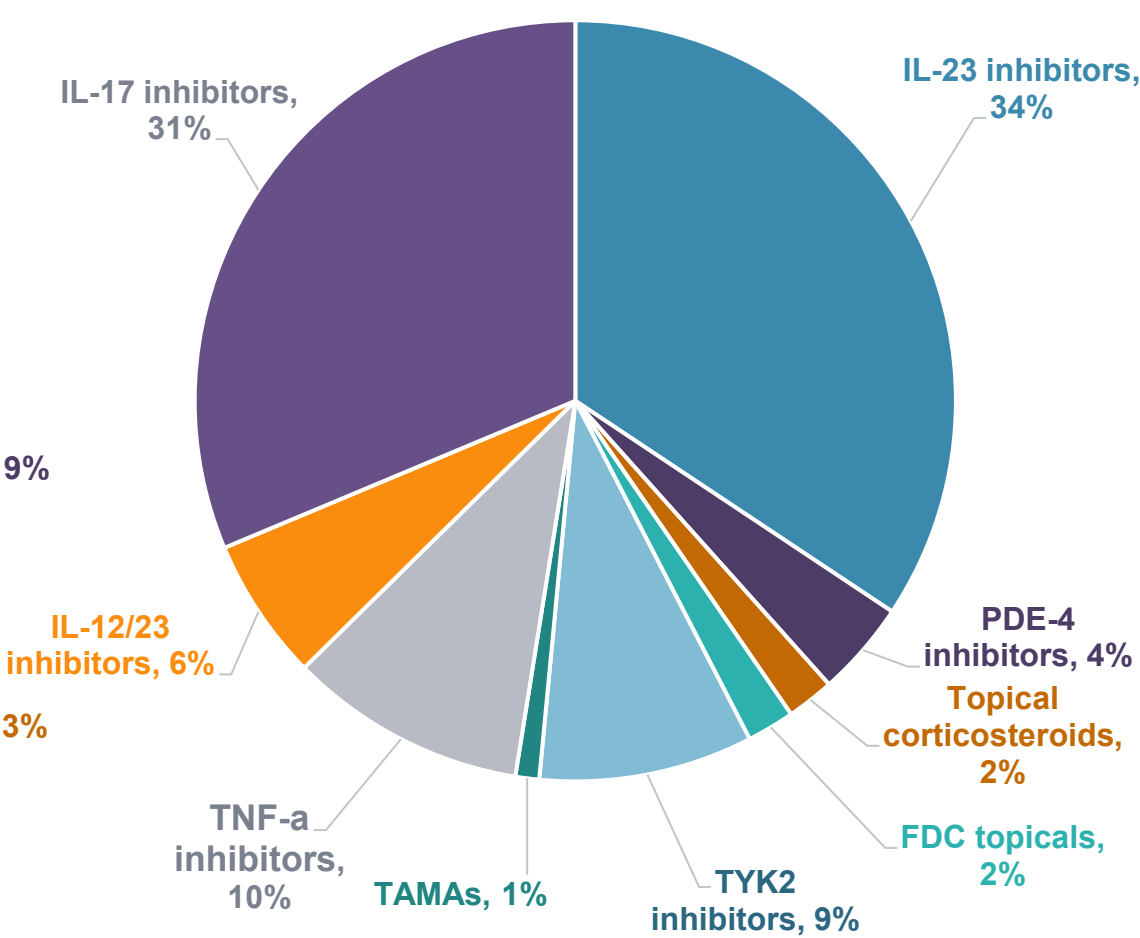
2021 DISTRIBUTION

Market Size: \$21.7B



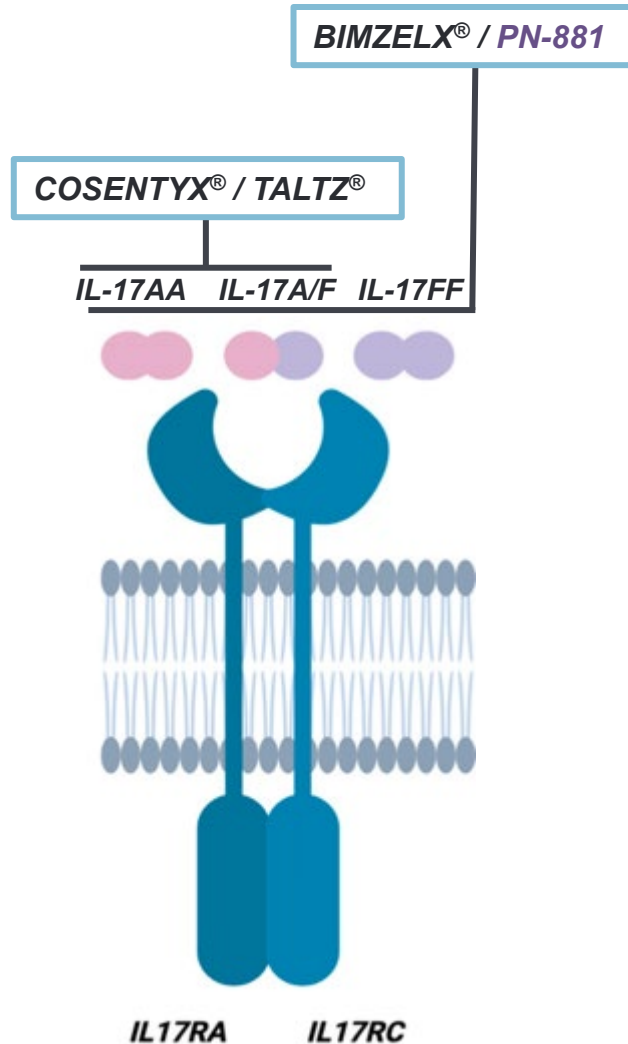
2031 DISTRIBUTION

Market Size: \$30.1B



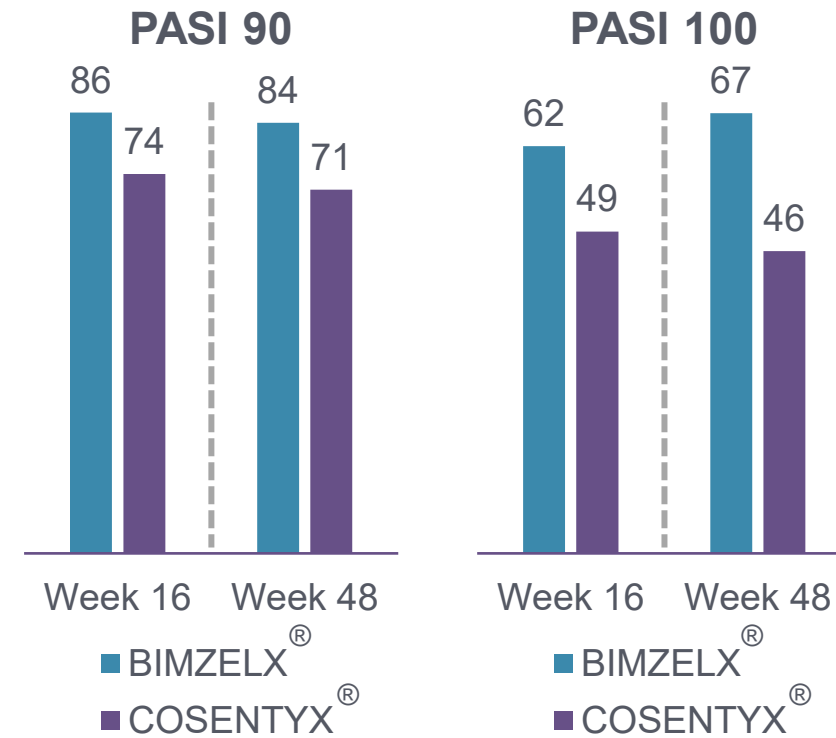
IL-17 Receptor Activated by Three Dimeric Forms of IL-17: IL-17AA, AF, and FF¹

Oral PN-881 Designed to Inhibit IL-17AA, AF, and FF



BE RADIANT Clinical Trial:

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



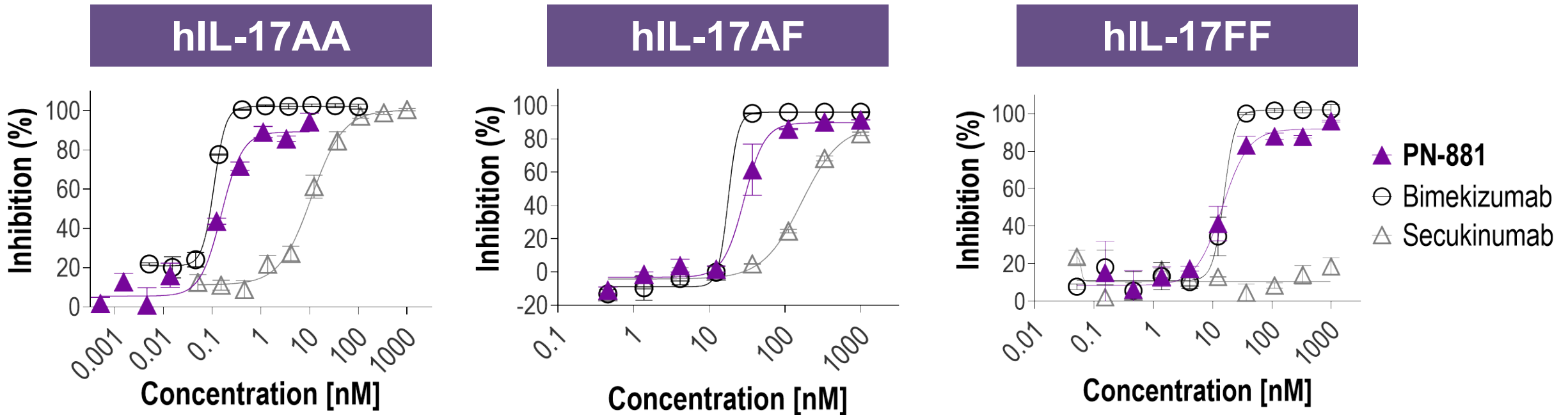
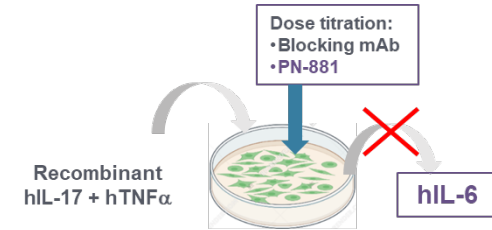
Criteria for Nomination of Oral PN-881 Development Candidate¹

Oral PN-881 Achieved all the Criteria for a Development Candidate Nomination

Attribute	Criteria
Potency	• Sub-nM potency vs. IL-17 AA • Blocks all 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
PK	• Oral exposure and half-life in rodent and higher species sufficient for oral daily dosing
PD model	• Mouse hIL-17 challenge, CXCL1 model
Efficacy Model	• Rat IL-23-induced skin inflammation model

PN-881 Inhibits IL-17-induced IL-6 Responses With Similar Potency as Bimekizumab in Primary Human Dermal Fibroblast (HDFn) Assay¹

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



PN-881 Potently Inhibits IL-17AA and IL-17FF¹

Similar Potency to Bimekizumab and ~70-fold More Potent Than Secukinumab

PN-881 vs Competitors	Neonatal Human Dermal Fibroblast (nHDF) and Human HT-1080 Fibrosarcoma Cell Line (HT-1080) IC ₅₀ s (nM)					
	IL-17 AA		IL-17 AF		IL-17 FF	
	nHDF	HT-1080	nHDF	HT-1080	nHDF	HT-1080
Oral Agents						
PN-881	0.15	0.13	29	27	15	14
DC-806 ² (or close analogue)	109	228	ND	ND	Inactive	Inactive
Injectable Agents						
Bimzelx [®]	0.12	0.17	18	19.5	14	13
Cosentyx [®]	10	11	175	151	Inactive	Inactive

ND, not determined.

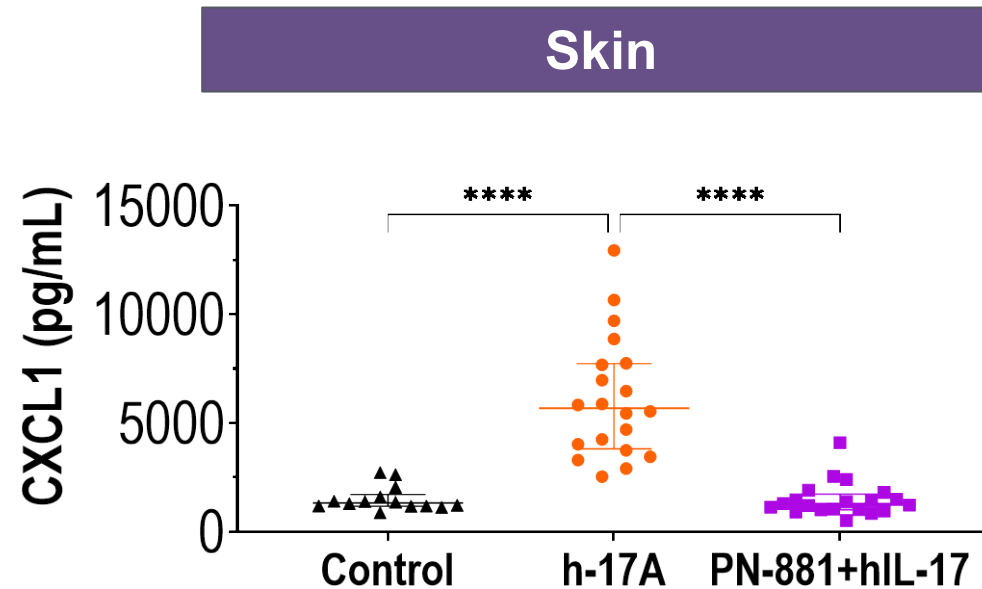
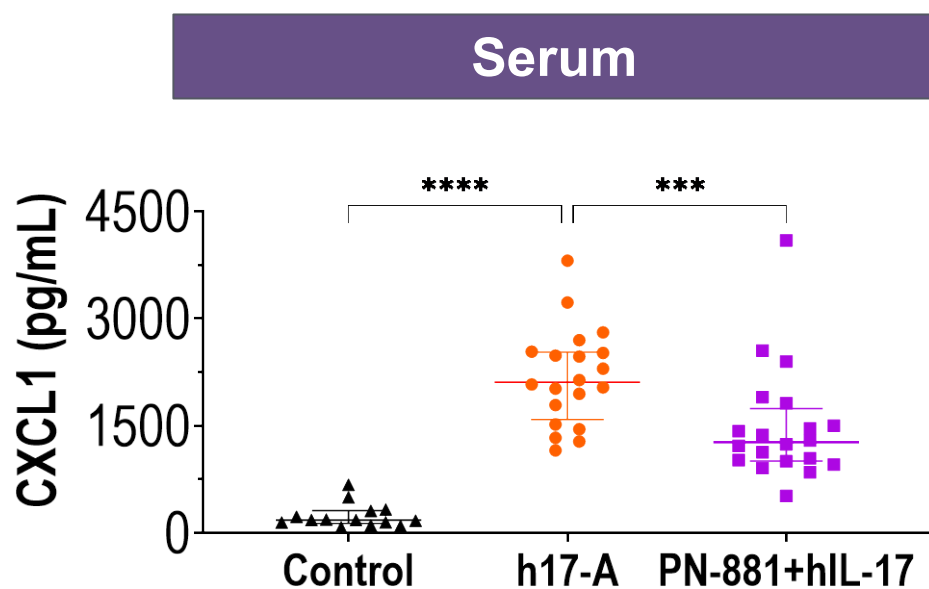
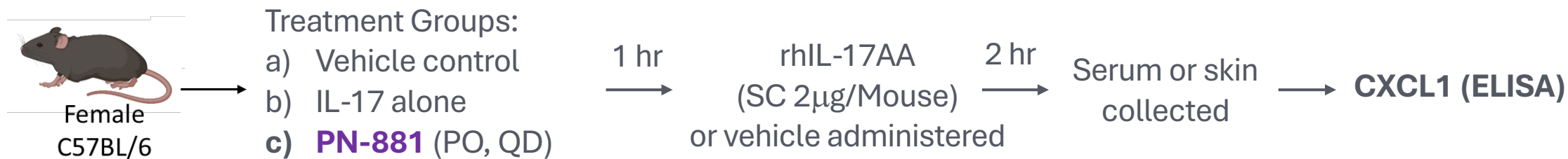
1. Adapted From Manrique M, et al. Presented at the European Academy for Dermatology and Venereology (EADV) Congress. September 17-20, 2025, Paris, France.

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

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

Oral PN-881 Neutralizes Human IL-17 in Mouse IL-17 Challenge PD Model¹

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

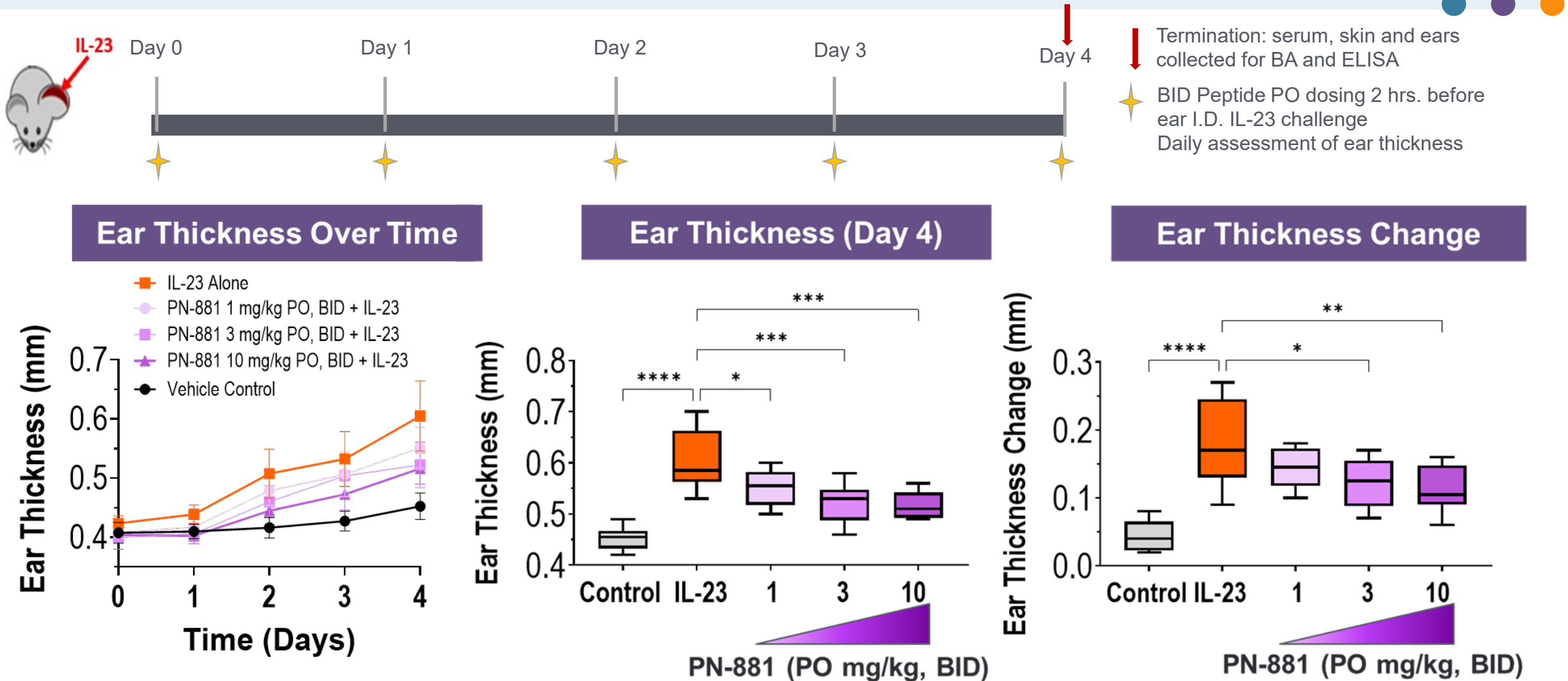


p<0.001, *p<0.0001 dot plot depict median and interquartile ranges

- 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 Model¹

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



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 (NCT07153146): Five-Part Phase 1 Study in Healthy Human Volunteers

Healthy Human Volunteers

N = 142 (estimated)

Eligibility:

- 18-65 years old
- Healthy male and female participants of non-childbearing potential
- Body mass index (BMI): 18-32 kg/m² (inclusive) at screening
- Male participants with female partners of childbearing potential must agree to use highly effective contraception during the study and for 90 days after the last dose

Primary endpoint:

- Incidence and severity of treatment-emergent adverse events (predose to 7 days after last dose)

Secondary endpoints:

- Pharmacokinetic and pharmacodynamic measurements

Part 1: Single Ascending Dose (SAD) (Randomized to PN-881 or Placebo)

Study Start Date: Oct '25

Additional Dosing Levels

Dose Level S1

Part 2: Multiple Ascending Dose (MAD) (Randomized to PN-881 or Placebo)

Additional Dosing Levels

Dose Level M1

Part 3: Assessment of Solid Dose Formulation

Part 4: Effect of Food on Solid Dose Formulation

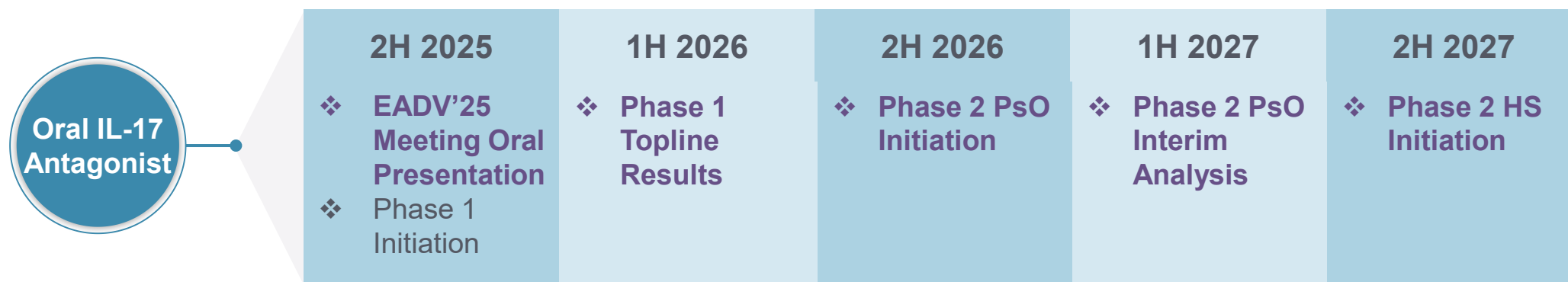
Part 5: Multiple Dose Pharmacokinetics of Solid Dose Formulation

Primary Completion Date: Jun '26

What We Hope to Learn from the PN-881 Phase 1 Study

- Safety and tolerability profile of PN-881 following single and multiple dosing
- Assess PN-881 pharmacokinetics to support once-daily dosing
- Selection of tablet formulation to progress into phase 2 studies
- PN-881 exposures will guide doses for phase 2 and design of the phase 2 study

PN-881: Near-Term Clinical Development Plan



PN-477: A Novel GLP-1R/GIPR/GCGR Triple Agonist Peptide Development Candidate

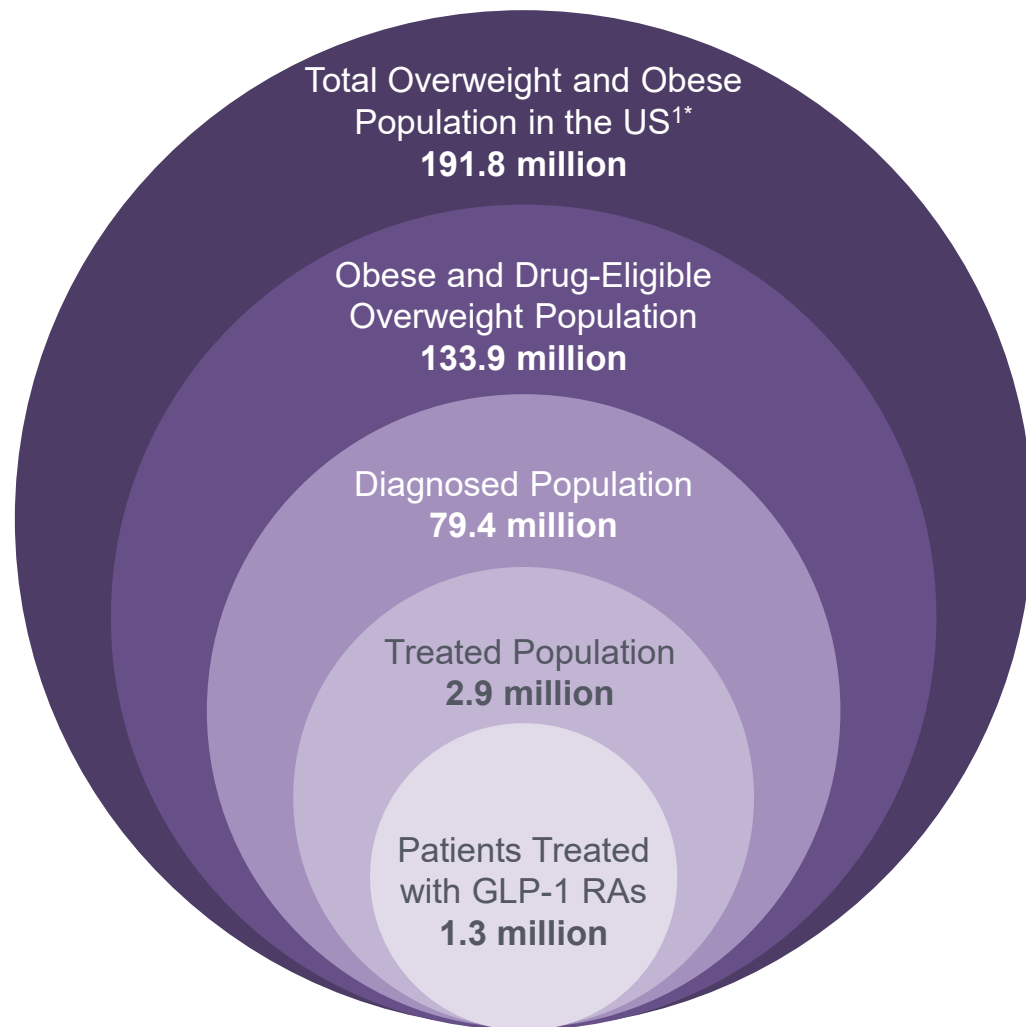
GLP-1R: Glucagon-Like Peptide-1 Receptor

GIPR: Gastric Inhibitory Polypeptide Receptor

GCGR: Glucagon Receptor

Obesity: Unprecedented Pharmaceutical Opportunity in the US and Worldwide

Only ~2% of Eligible Patients Receive Drug Treatment



- Obesity is a global epidemic
 - In 2024, nearly **40% of Americans were obese or considered drug-eligible overweight**¹
- Approved drugs: Injectable peptides
- Current challenges with anti-obesity drugs¹
 - Early days & limited options
 - Adverse effects
 - Convenience; needle avoidance
- **‘Oral’ and ‘more effective’ agent an attractive option for a chronic condition**

Desirable Features for Next Generation Anti-Obesity Candidate

- Currently approved therapies are injectables
 - Semaglutide (Wegovy®): Mono GLP-1R agonist – 13.7% body weight loss¹
 - Tirzepatide (Zepbound®): Dual GLP-1R and GIPR agonist – 20.2% body weight loss¹
- Retatrutide: An injectable triple agonist in Ph 3 development



***Proprietary Peptide
Technology***

An ORAL Triple-Agonist Peptide (GLP-1R/GIPR/GCGR)

- Potential improvements
 - **Oral option**
 - Magnitude of body weight loss
 - Potential secondary benefits in co-morbidities (diabetes, CVD, OSA, CKD, MASH etc.)
 - Improving tolerability: mainly GI (nausea, vomiting)
 - Favorable fat vs. lean mass loss

PN-477: A Novel Triple GLP/GIP/GCG Receptors Agonist Peptide

Optionality for Oral or Subcutaneous Dosing



PN-477_o

**ORAL Triple-Agonist
Once-daily Dosing**



PN-477_{sc}

**Injectable Triple-Agonist
Once-weekly Dosing**

PN-477 Triple Agonist (GLP-1R, GIPR, GCGR) Peptide as Development Candidate

Novel Chemical Entity, Oral Triple Agonist, Potent, and Stable in GI Fluids

Attribute	Criteria
Potency	• nM potency vs GLP-1R, GIPR, GCGR ✓
Stability	• Stable in simulated gastric and intestinal fluids ✓ • Stable in serum ✓ • Metabolic stability ✓ • Thermostability ✓
Efficacy Model	• Mouse Diet Induced Obesity (DIO) model ✓
<i>in vivo</i> Pharmacodynamics	• Glucose control with glucose tolerance test ✓
<i>in vivo</i> Pharmacokinetics	• Oral bioavailability demonstrated in mouse, rat, dog, cynomolgus monkey ✓ • GI stability supports once-a-day oral dosing ✓ • Plasma PK profile supports once-a-week subcutaneous dosing ✓

PN-477: A Highly Potent Triple GLP-1/GIP/GCGR Receptor Agonist Designed to Provide Weight Loss Profile of Retatrutide and GI Tolerability of Tirzepatide

	Human EC ₉₀ (nM)			Mouse EC ₉₀ (nM)		
	GLP-1R	GIPR	GCGR	GLP-1R	GIPR	GCGR
Semaglutide ^{1,‡} (Novo Mono GLP-1R)	74	NA [†]	NA [†]	6.1	NA [†]	NA [†]
Tirzepatide ^{2,‡} (Eli Lilly Dual GLP-1R/GIPR)	269	16	NA [†]	21	867	NA [†]
Retatrutide ^{3,‡} (Eli Lilly Triple GLP-1R/GIPR/GCGR)	103	17	83	8.3	493	102
PN-477	49	2.7	56	17	133	1092

‡Sourced from MCE Cat. HY-114118 (Semaglutide); 1PlusChem Cat. 1P01MVTY (Tirzepatide); MCE Cat. HY-P3506 (Retatrutide)

[†] NA: Not Active

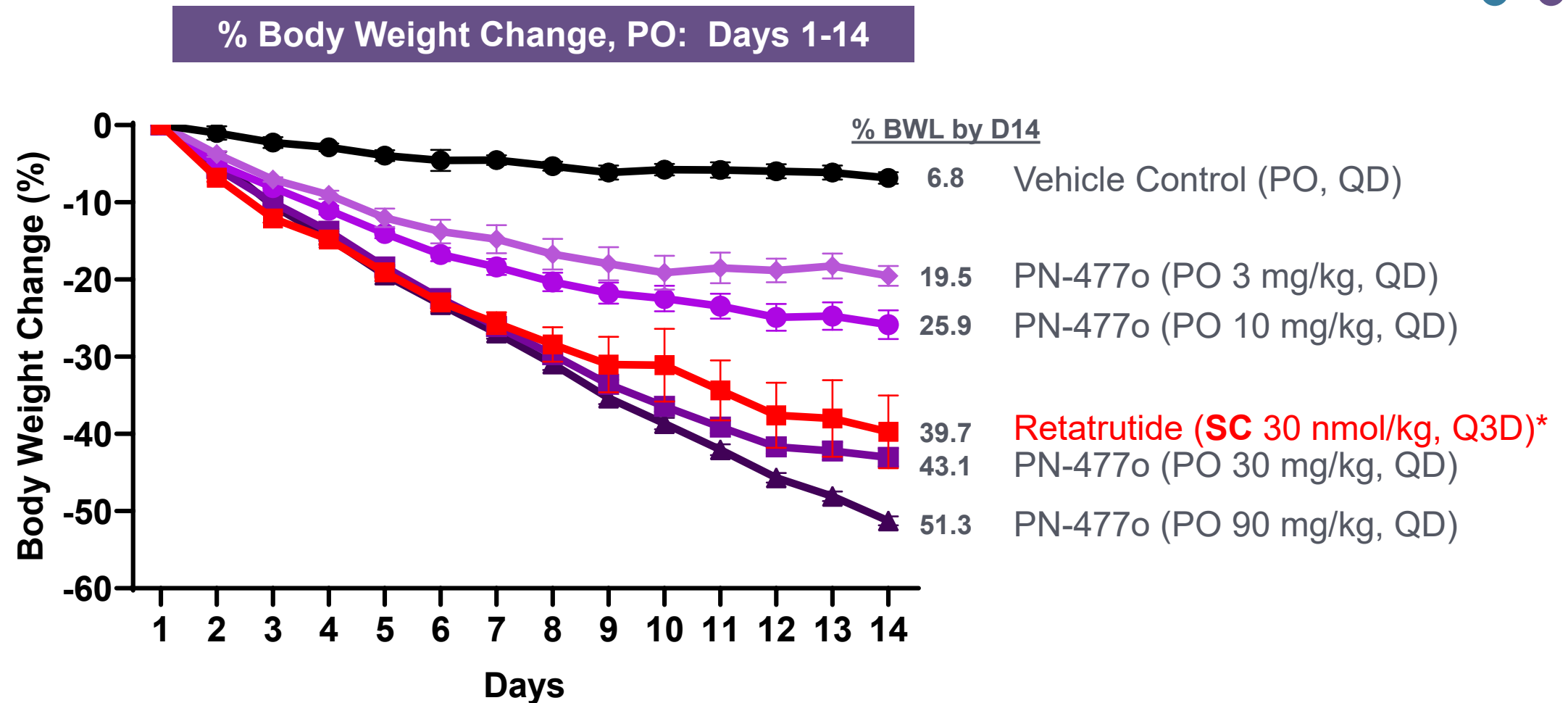
- Human EC₅₀ potencies:

Human EC ₅₀ (nM)	GLP-1R	GIPR	GCGR
PN-477	4.6	0.39	15
Retatrutide	12.2	1.5	21

- Higher GIPR potency may be favorable for better GI tolerability^{4,5}

Dose Proportional Body Weight Loss of Up to 50% with Oral PN-477o

DIO Mice Study #1



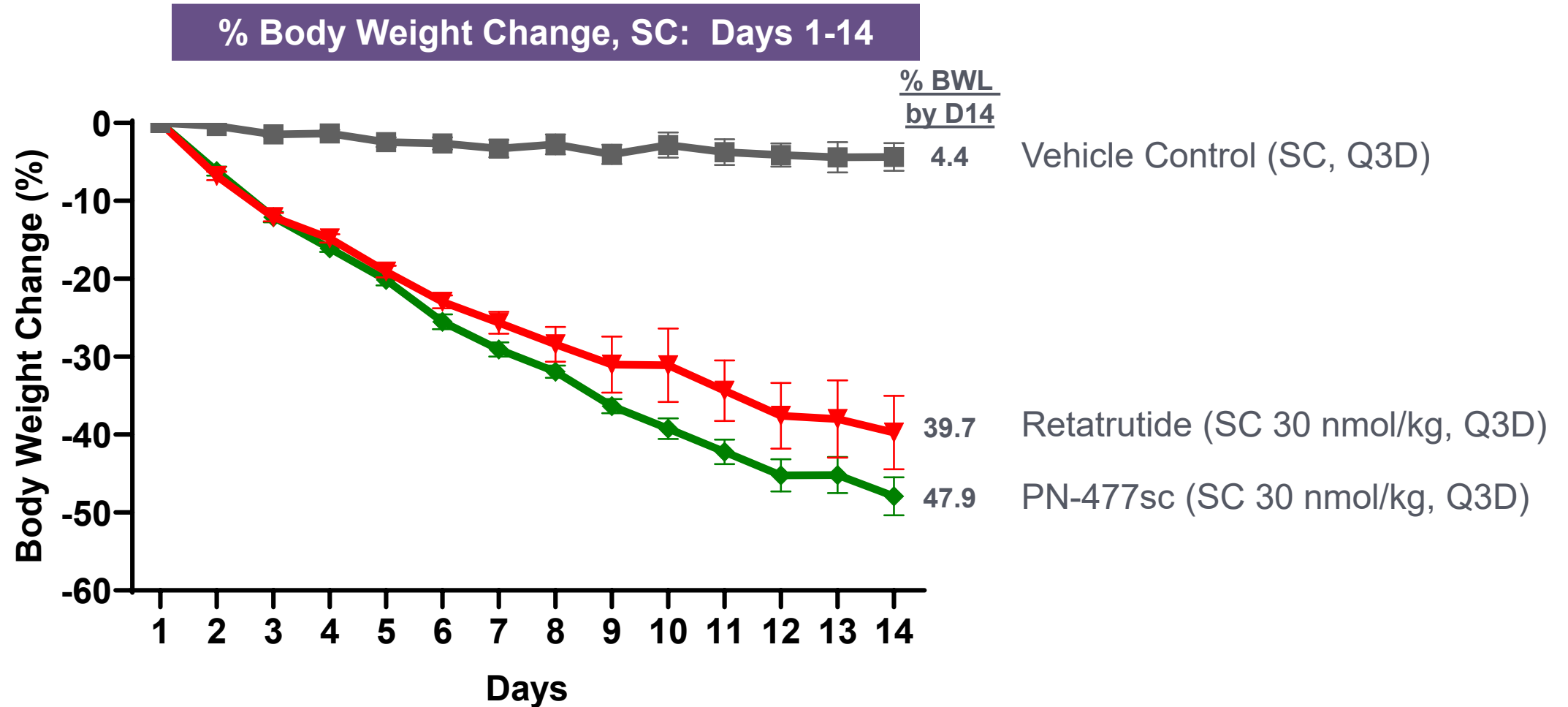
* Retatrutide SC 30 nmol/kg dose is the highest dose reported for DIO mouse efficacy study

(Cell Metabolism 34, 1234–1247, September 6, 2022)

BWL: Body Weight Loss; DIO: Diet Induced Obese; Data points depict mean $\pm$ SEM. PO = per os (oral), SC = subcutaneous, QD = once a day, Q3D = every 3 days

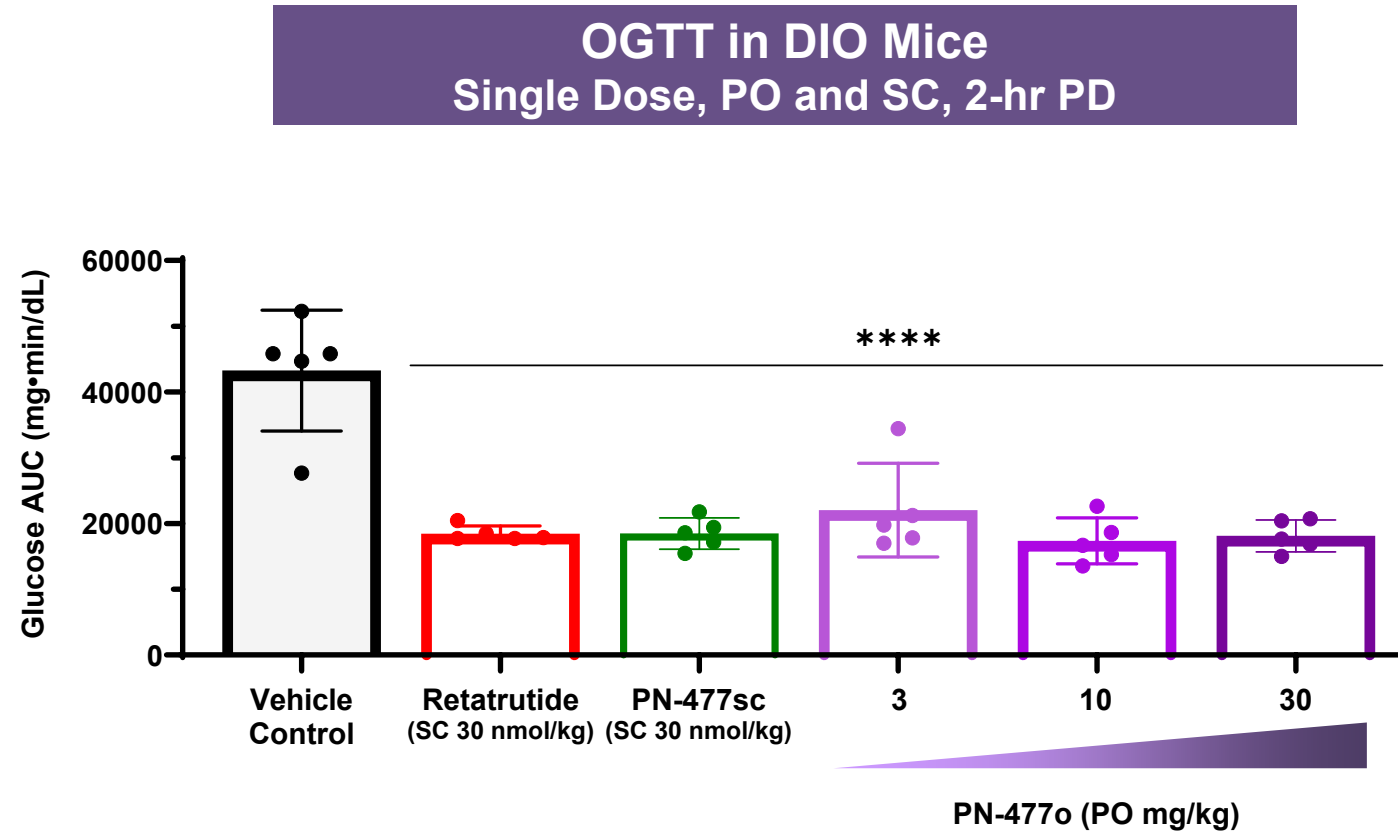
Subcutaneous PN-477sc Achieves Body Weight Loss Comparable to Retatrutide

DIO Mice Study #1



PN-477 (Oral and SC) Improves Glycemic Control after Glucose Challenge

DIO Mice Study #3

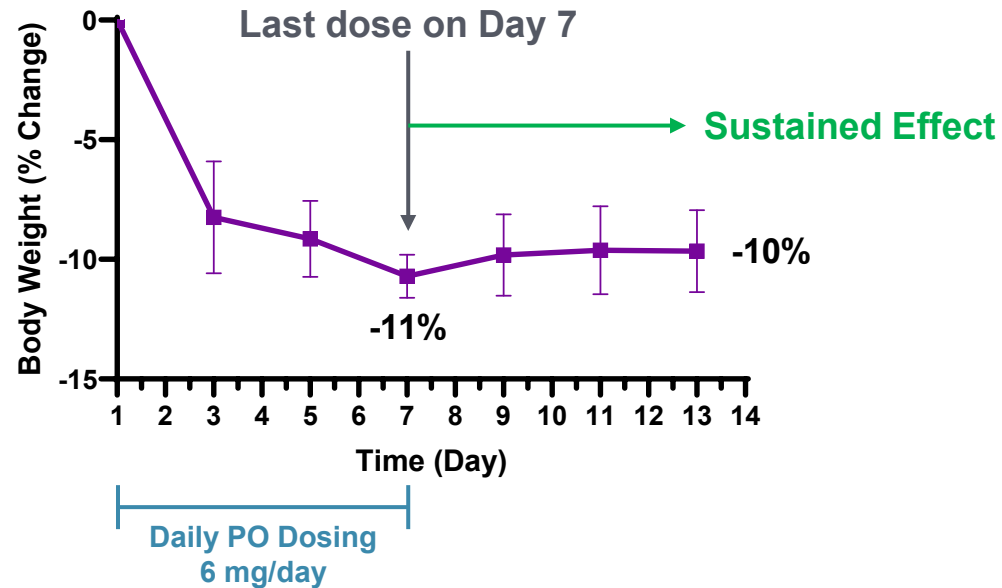


- Glycemic control is significantly improved in DIO mice after PN-477 PO or SC when compared to the vehicle control
- Profiles consistent with retatrutide

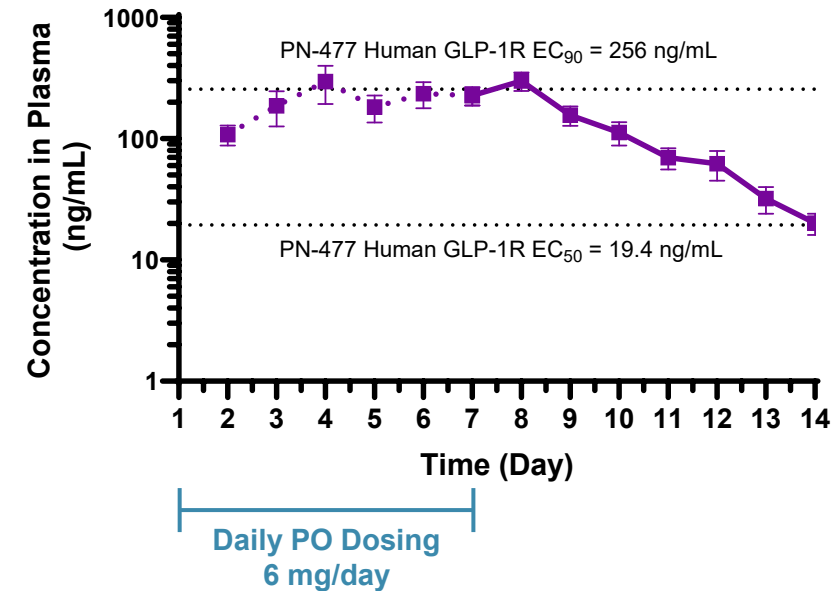
11% BW Loss by Day 7 in Cynomolgus Monkeys after 7-Day Oral Dosing of PN-477o

Weight Loss Sustained for 6 Days After Last Dose

Cyno % BW Change, PO



Cyno PK C_{trough} Day 1-7, PO

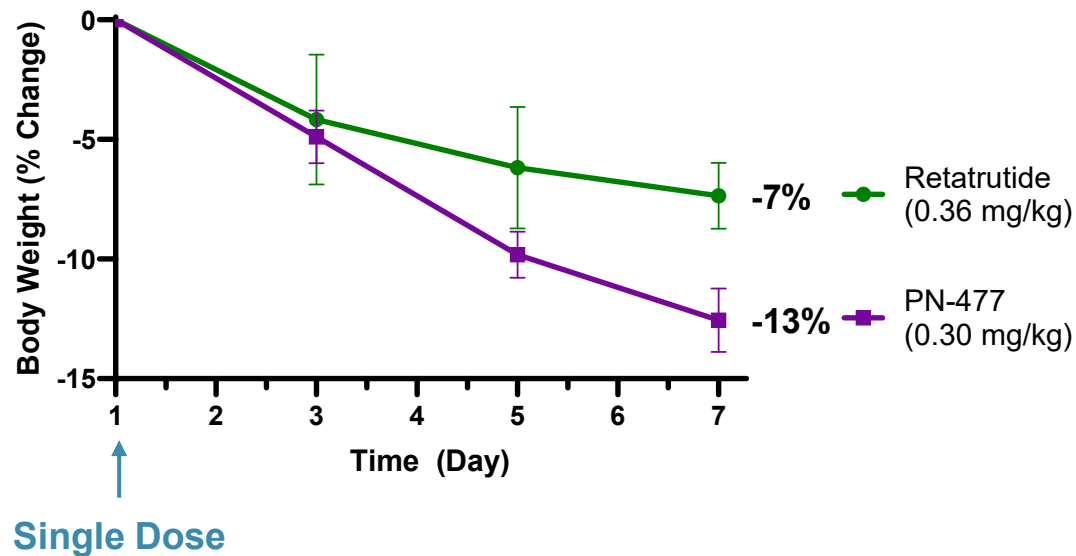


- PN-477o PK profile suggests once daily human dosing
- Body weight loss was sustained for 6 days post-last dose

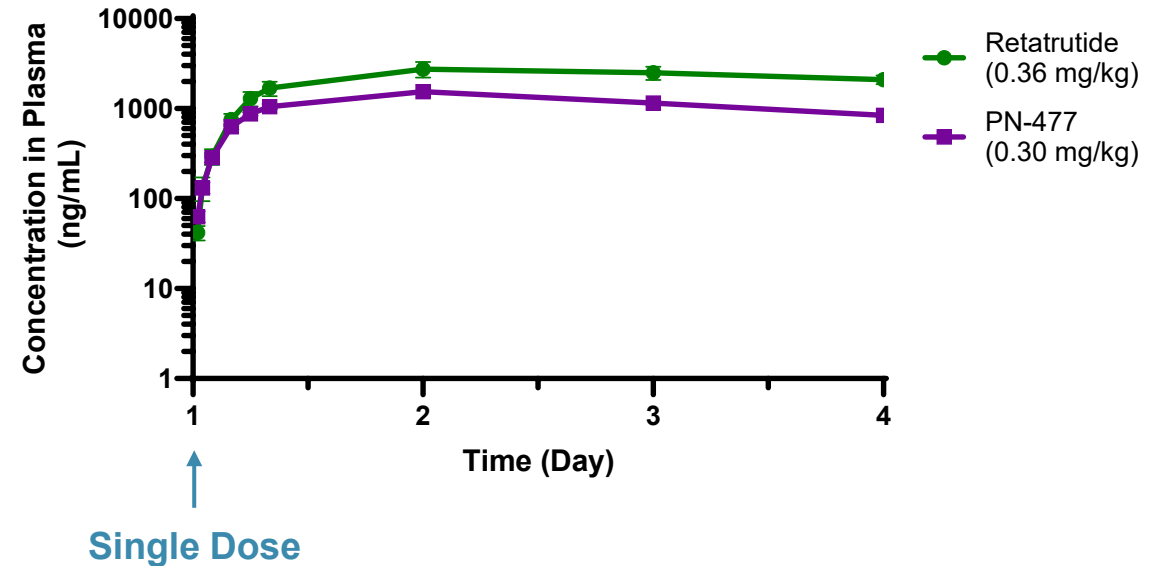
13% BW Loss by Day 7 in Normal Monkeys after Single SC Dose of PN-477

PN-477 Vs. Retatrutide

Cyno % BW Change, SC



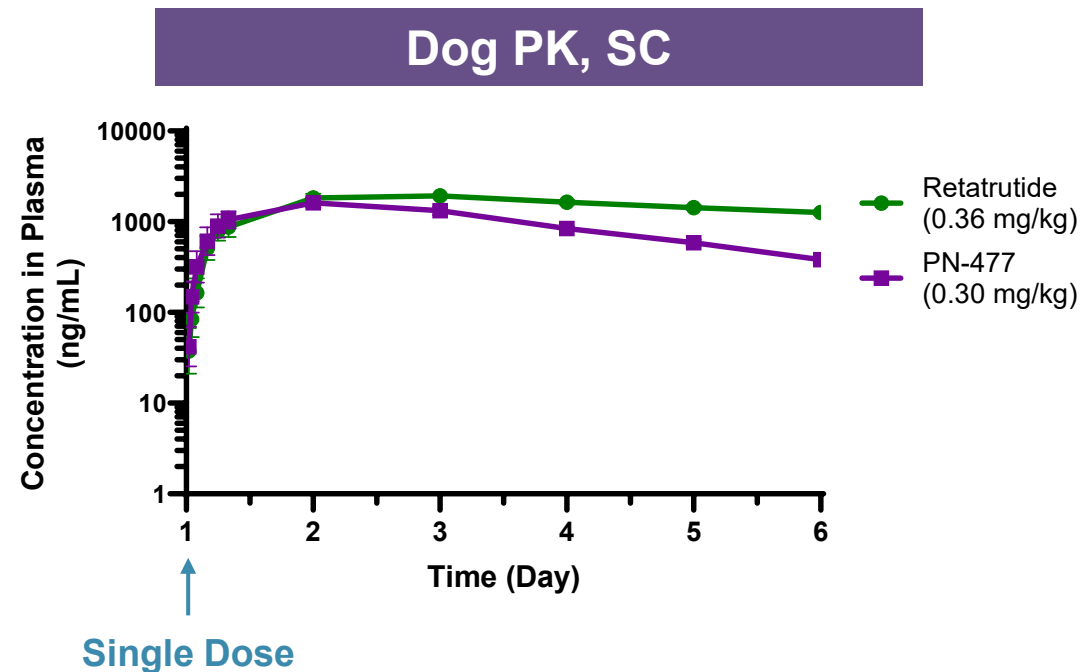
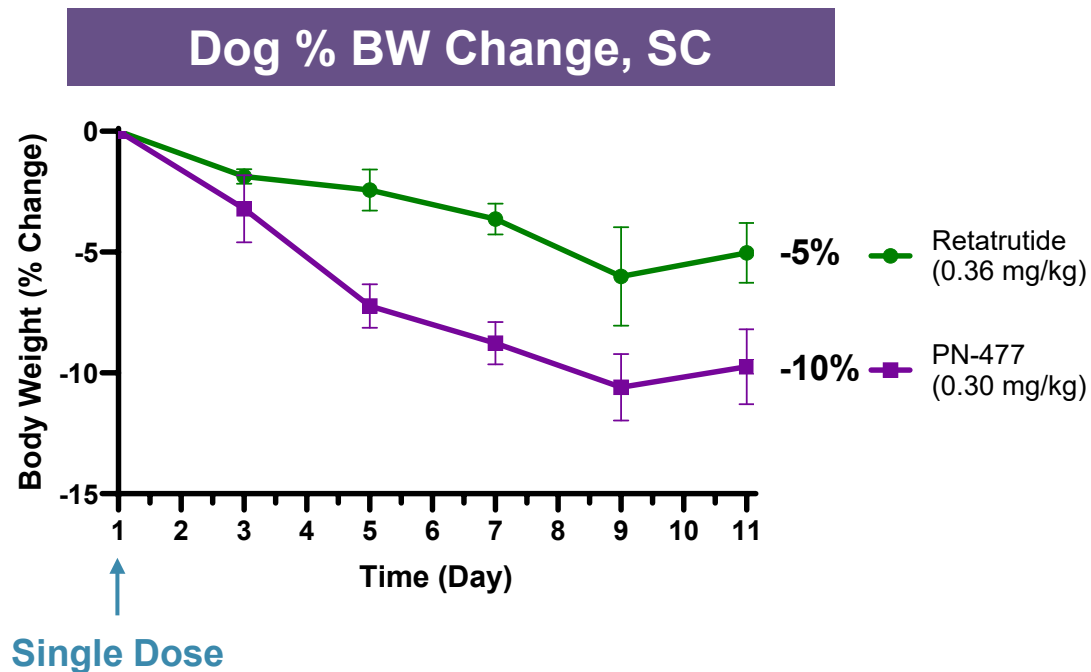
Cyno PK, SC



PN-477sc PK profile suggests once weekly human dosing

10% BW Loss by Day 11 in Normal Beagle Dogs after Single SC Dose of PN-477

PN-477 Vs. Retatrutide



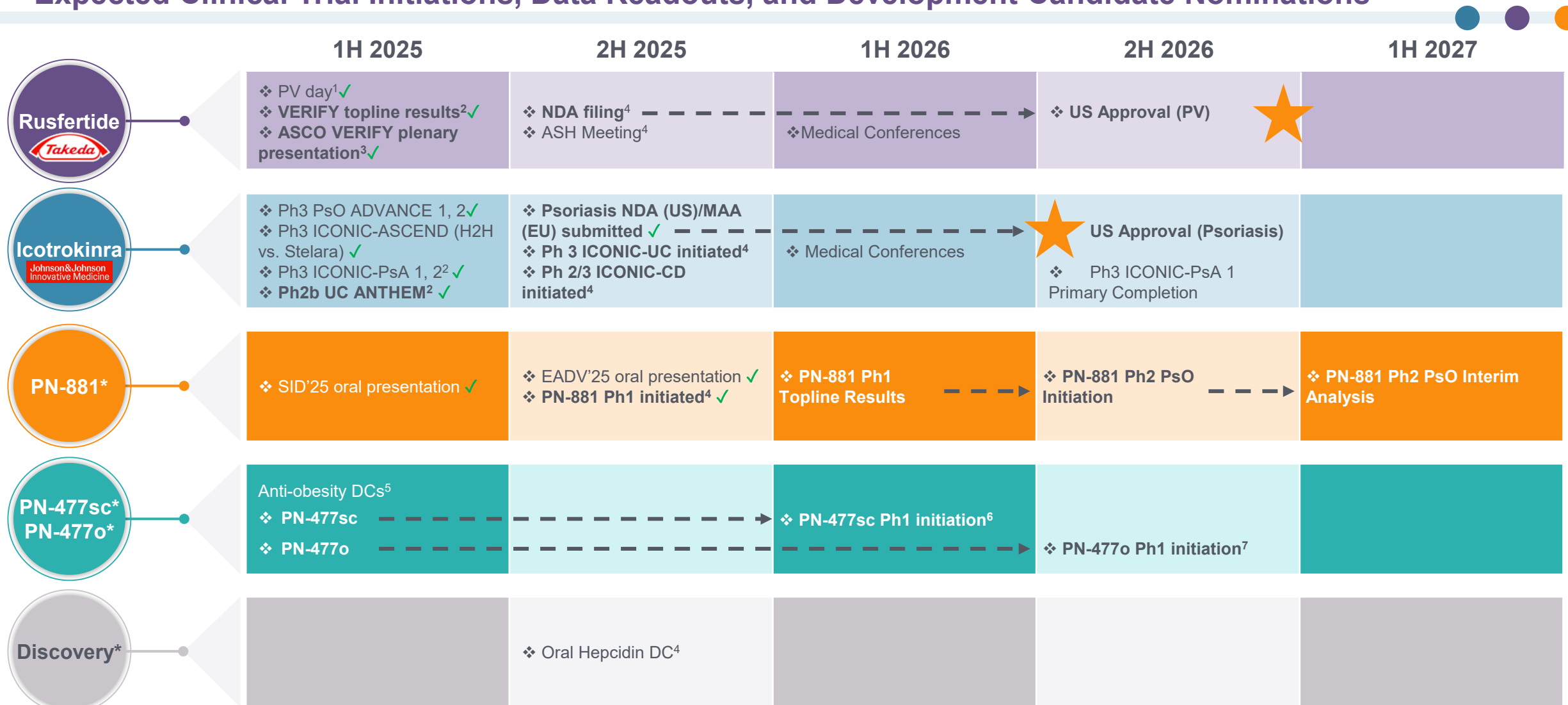
PN-477sc PK profile suggests once weekly human dosing

PN-477: A Potential Best-in-Class Triple Agonist Anti-Obesity Peptide Development Candidate with Convenience of Once-Daily Oral and Once-Weekly SC Dosing

- Novel, orally stable, and potent triple agonist (GLP-1R, GIPR, GCGR)
- Engineered balance of GLP-1R, GIPR, GCGR absolute and relative potencies
 - Designed to provide maximal weight loss and optimal body composition of retatrutide and GI tolerability of tirzepatide
- Weight loss in DIO mice benchmarks favorably versus retatrutide
 - Dose-proportional body weight loss of up to 50% in DIO mouse model achieved with oral administration of PN-477o
 - PN-477sc provides similar body weight loss as retatrutide with equivalent SC dose
 - Preferential fat mass to lean mass loss observed; similar to retatrutide
- Weight loss after single dose of PN-477sc benchmarks favorably versus retatrutide in normal dogs and monkeys
- PK profiles after Oral and SC dosing in normal dogs and monkeys support:
 - **PN-477o**: Once-daily ORAL Triple-Agonist Peptide
 - **PN-477sc**: Once-weekly injectable Triple-Agonist Peptide
- IND-enabling studies underway

Major Upcoming Catalysts in 2H 2025 Through 1H 2027

Expected Clinical Trial Initiations, Data Readouts, and Development Candidate Nominations





Thank you