Protagonist Therapeutics

COMPANY OVERVIEW

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

November 9, 2026



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This presentation and any accompanying oral presentation contain forward-looking statements within the meaning of the Private Securities Litigation Reform Act. All statements other than statements of historical facts contained in this presentation are forward-looking statements, including statements regarding: our potential receipt of milestone and royalty payments from Takeda and J&J; market potential for MIMRYLO™ (rusfertide) and ICOTYDE® (icotrokinra); actions of the U.S. Food and Drug Administration ("FDA") and foreign regulatory agencies; timing and results related to our pre-clinical and clinical product candidates (including PN-881, PN-477, PN-458, and PN-8047, among others); and the scope of protection we are able to establish and maintain for intellectual property rights covering our product candidates. 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.

Forward-looking statements are subject to risks and uncertainties, including those discussed in our filings with the Securities and Exchange Commission, including in the "Risk Factors" and "Management's Discussion and Analysis of Financial Condition and Results of Operations" sections of our most recently filed periodic reports on Form 10-K and Form 10-Q and subsequent filings and in the documents incorporated by reference therein. Because forward-looking statements are inherently subject to risks and uncertainties, some of which cannot be predicted or quantified and some of which are beyond our control, you should not rely on these forward-looking statements as predictions of future events. The events and circumstances reflected in our forward-looking statements may not be achieved or occur and actual results could differ materially from those projected in the forward-looking statements. The information included in these materials is provided as of the date specified on the cover page of this presentation, unless specified elsewhere herein, and is qualified as such. Except as required by applicable law, we undertake no obligation to update any forward-looking statements or other information contained herein, whether as a result of any new information, future events, changed circumstances or otherwise.

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ICOTYDE® and MIMRYLO™ Revenue Engine Drives R&D Pipeline Development

Targeting Combined Addressable Markets >$100 Billion

Revenue Engine

Commercial & Partnered

ICOTYDE® (icotrokinra)
Oral IL-23R Antagonist • Partner: J&J

FDA Approved: Q1 ’26
China, Japan & EC approval: Q3 ’26
Moderate-to-Severe Plaque Psoriasis

6–10% royalties + milestone payments
>$10B peak potential[1]

MIMRYLO™ (rusfertide)
SC Hepcidin Mimetic • Partner: Takeda

FDA Approval: Aug ’26
UAE Approval: Sep ’26
Polycythemia Vera

14–29% royalties + milestone payments
$1-2B peak sales[2]

Wholly-Owned Pipeline

Inflammation & Immunology

Oral PN-881 · IL-17A/F
Ph1 completed
Ph2b initiation in psoriasis: Q1 ’27
Potential Indications: PsO, PsA, HS, SpA

Oral IL-4Rα Antagonist
Lead optimization
Potential Indications: AD, Asthma

Metabolic

Oral PN-477 · GLP/GIP/GCG
SC Ph1 complete; Oral Ph1: 1H ’27

Oral PN-458 · GLP/GIP
IND enabling studies

Amylin Mono/Poly-Agonists
Lead optimization

Hematology

Oral PN-8047 · Hepcidin Mimetic
Ph1: Q1 ’27
Potential Indication: Polycythemia Vera

Protagonist Therapeutics

1. HSBC Dec 2025 Consensus Forecast (across all indications); 2. Takeda 44th Annual J.P. Morgan Healthcare Conference corporate presentation 2026.

Strong Financial Position and Anticipated Future Cash Flows

Supports Aggressive Development of our R&D Portfolio and Potential Capital Return



CASH, CASH EQUIVALENTS & MARKETABLE SECURITIES

$834.6M

as of September 30, 2026



ADDITIONAL PAYMENTS TRIGGERED UPON MIMRYLO APPROVAL

$275M

Received in October 2026

$200M remaining opt-out payment and $75M FDA approval milestone



POTENTIAL FUTURE CASH INFLOWS FROM PARTNERSHIPS

~$1.5B

Potential Future milestones
+
6-10% royalties on ICOTYDE
+
14-29% royalties on MIMRYLO

Protagonist Therapeutics

Takeda and J&J Partnership Economics

ICOTYDE® (icotrokinra); Oral IL-23R Antagonist; Partner: J&J

$387.5M	$580M	6–10%	>$10B[1]
Payments earned	Potential future milestones	Tiered worldwide royalties	ICOTYDE peak sales potential

FDA Approved Mar ’26 (Mod to Sev Plaque PsO) · PsA Ph3 · UC Ph3 · CD Ph2/3 · China (NMPA) Approved Aug ’26 · EC Approval/MA: Sept ’26
7.25% weighted-avg royalty through $4B; 10% for annual sales ≥$4B

MIMRYLO™ (rusfertide); SC Hepcidin Mimetic; Partner: Takeda

$800M	$875M	14–29%[2]	$1–2B[3]
Payments earned to date	Potential future milestones	Tiered worldwide royalties	Takeda-guided peak sales

FDA Approved Aug ‘26 (PV) · Ph3 VERIFY PV study met primary + all 4 key secondary endpoints
21% weighted-avg royalty through $1.5B; 29% for annual sales ≥$1.5B

~$1.2B in upfront, milestone, and opt-out payments earned through September 30, 2026

Protagonist Therapeutics

EC, European Commission; MA, Marketing Authorization. 1. HSBC Dec 2025 Consensus Forecast (across all indications); 2. 1% royalty payable to Zealand Pharma; 3. Takeda 44th Annual J.P. Morgan Healthcare Conference corporate presentation 2026.
ICOTYDE is a registered trademark of Johnson & Johnson and its affiliates.

Multiple Programs With Significant Value Creation Over the Next 24 Months

PROGRAM	THERAPEUTIC AREA	STAGE / STATUS	VALUE INFLECTION
ICOTYDE® Oral IL-23R	I&I	**Approved for Mod to Sev Plaque PsO**	Launch trajectory Ph2 and Ph3 readouts
MIMRYLO™ Hepcidin mimetic	Hematology	**Approved for Erythrocytosis in PV**	Launch trajectory
PN-881 Oral IL-17A/F	I&I	**Ph1; Ph2b PsO**	Ph1 safety/PK completion ✓ Ph2b PsO dose finding/PoC
PN-477 Oral triple agonist	Metabolic	**Ph1 Oral**	Ph1 SC SAD PoC ✓ Ph1 Oral SAD/MAD (7-day) Ph1b Oral MAD (13 weeks) PoC
PN-458 Oral dual agonist	Metabolic	**Ph1 start planned**	Ph1 Oral SAD/MAD
PN-8047 Oral hepcidin	Hematology	**Ph1 start planned**	Ph1 SAD/MAD PD PoC Ph2 PV study
Discovery IL-4Rα; amylin	Discovery	**Candidate selection**	Multiple development candidates

… targeting combined addressable markets >$100bn

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IL, interleukin; MAD, multiple ascending dose; PD, pharmacodynamics; PK, pharmacokinetics; PoC, proof of concept; PsO, psoriasis; PV, polycythemia vera; SAD, single ascending dose; SC, subcutaneous.

Protagonist Therapeutics

Business Overview

- **Commercial Assets**
  - ICOTYDE
  - MIMRYLO
- **De-risked Strategy and Strengthened Pipeline**
  - De-risked targets (e.g., IL-17, IL-4, hepcidin, incretin, glucagon and amylin)
  - Validated platform and approach (ICOTYDE, MIMRYLO)
- **Accelerated Path to Clinical Proof of Concept (PoC)**
  - Ph1 PoC planned for obesity and oral hepcidin programs
  - Well-established clinical PoC pathway in I&I programs
- **Non-Dilutive Funding Model**
  - $834.6M cash (3Q26)
  - Royalty streams from ICOTYDE (6–10%) and MIMRYLO (14–29%), plus milestone payments
  - No expected equity raise in the foreseeable future
  - $300M share buyback announced September 2026

Protagonist Therapeutics

ICOTYDE® (icotrokinra; JNJ-2113, formerly PN-235): Targeted Oral IL-23 Receptor Antagonist Peptide

Setting a new standard of treatment in moderate to severe plaque psoriasis and other IL-23 mediated diseases

J&J Partnership: 2017 to Present



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ICOTYDE® (icotrokinra): First Oral IL-23R Therapy Targeting >$80B[1] Market

THE INNOVATION

- ***First- and only-in-class targeted ORAL peptide*** IL-23R antagonist in late-stage development
- **Four major indications:**
  - Moderate to severe plaque psoriasis (PsO); approved (US)
  - Psoriatic arthritis (PsA); Ph3 ongoing
  - Ulcerative colitis (UC); Ph3 ongoing
  - Crohn's disease (CD); Ph2b/3 ongoing

THE OPPORTUNITY

Ustekinumab	>$11B[2]
Guselkumab	>$10B[3]
Risankizumab	>$20B[4]

~90%

of patients receiving SC/IV therapy and willing to switch to an oral option with comparable safety and efficacy[5]

PsO / IBD patients eligible for advanced therapies but remaining untreated[6] ▶ **~50-70% (5M)**

>$10B[7] blockbuster potential

Established efficacy and proven safety profile in a once-daily pill

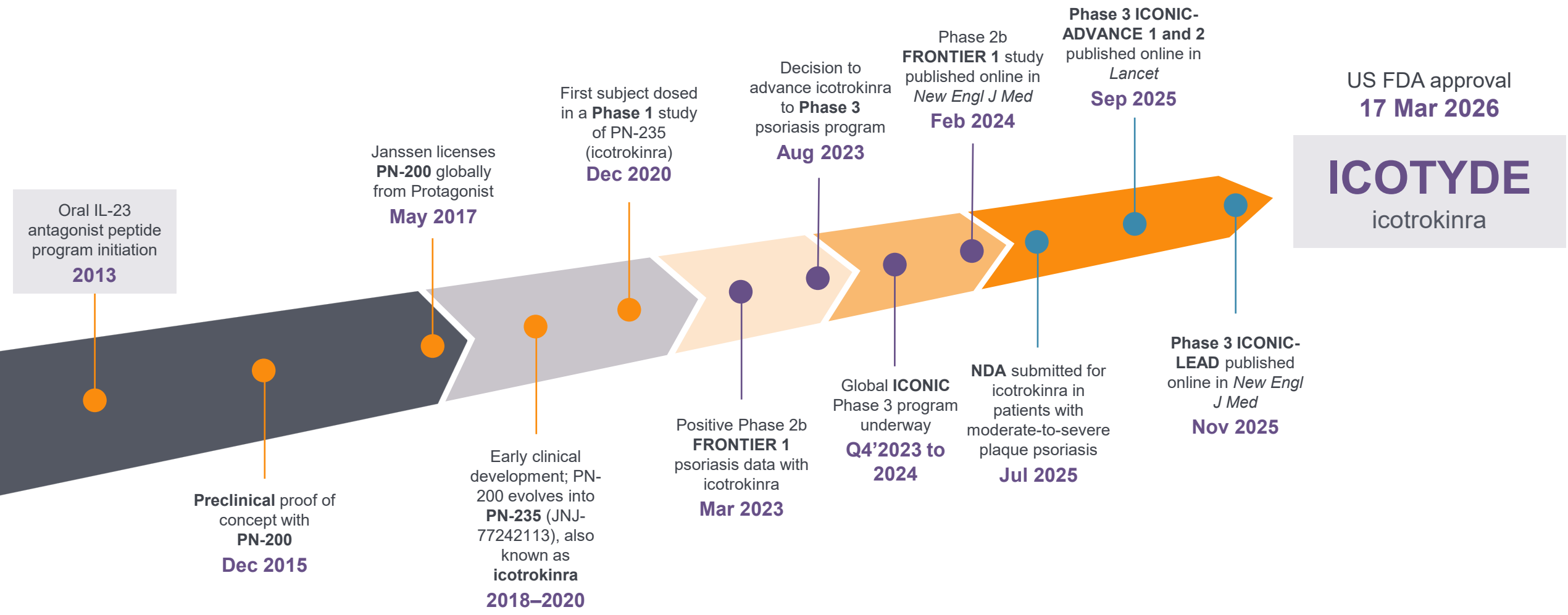
Protagonist Therapeutics

1. Evaluate 2030 projected market size for PsO, PsA, IBD, UC.
2. J&J reported sales in 2023 (peak year).
3. J&J Q2 earnings call, July 16, 2025.
4. Abbvie Full-year and Q4 2024 financial results, Jan 31, 2025.
5. Stein Gold L, et al., Presented at 2025 Fall Clinical Dermatology Conference, Oct 2025, Las Vegas, NV.
6. J&J remarks, Enterprise Day Presentation, Dec 2023.
7. HSBC Dec 2025 Consensus Forecast.

ICOTYDE is a registered trademark of Johnson & Johnson and its affiliates

ICOTYDE® (Icotrokinra, Formerly Known as JNJ-77242113 and PN-235)

From Discovery to FDA Approval



FDA, US Food and Drug Administration; NDA, New Drug Application.

ICOTYDE® (icotrokinra)

US FDA approval of ICOTYDE, formerly PN-235

- Johnson & Johnson partnership overview
  - 2017 to present
  - Protagonist completed pre-clinical and first Ph1 study[1]
  - J&J responsible for further development and commercialization

- ICOTYDE is the **first and only IL-23R targeted oral peptide** to clear skin for patients with moderate to severe plaque psoriasis, with a **favorable safety profile** and the **convenience of a once-daily pill**

- Approval supported by four phase 3 studies that met all primary endpoints and demonstrated a favorable safety profile in 2,500+ patients

1. Fourie, AM et al. JNJ-77242113, a highly potent, selective peptide targeting the IL-23 receptor, provides robust IL-23 pathway inhibition upon oral dosing in rats and humans. *Sci Rep* 2024(14):17515. https://doi.org/10.1038/s41598-024-67371-5.

ICOTYDE is a registered trademark of Johnson & Johnson and its affiliates

ICOTYDE Commercial Launch Performance and Recent Commentary

Launch Theme	Commentary
Launch Momentum	"**More than 20,000 patients** have initiated therapy through **nearly 9,000 prescribers** since ICOTYDE's launch in the U.S."
Patient Mix	"**Approximately 60% of the patients are systemic naïve**… roughly the 40% remaining, **20% are sourced from orals** and **20% are sourced from other treatments**, most likely biologics." –Tom Cavanagh, EVP, Worldwide Chairman, Innovative Medicine
Strategic Importance	"We do foresee ICOTYDE to be **one of our biggest assets in Innovative Medicine**, and it is **off to an incredibly great start**." –Tom Cavanagh, EVP, Worldwide Chairman, Innovative Medicine
Commercial Execution	"We continue to make **strong progress on commercial access**, with ICOTYDE now **broadly covered across all national plans**." – Joaquin Duato, Chairman and Chief Executive Officer

J&J Reported Launch Metrics[1]

~20K Patients initiated

~9K Prescribers

Broad Commercial Coverage

Patient mix

~60% systemic-naïve

~20% from other orals

~20% from other treatments, most likely biologics

> *"ICOTYDE, our first in class targeted oral peptide for plaque psoriasis, continues to outpace the recent competitors' launches."*
>
> Joaquin Duato, Chairman and Chief Executive Officer · Q3'26 Earnings Call

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[1]Johnson & Johnson Remarks, Q3 '26 Earnings Call, October 13, 2026.

Icotrokinra Potential Expansion of Multiple Indications in Coming Years

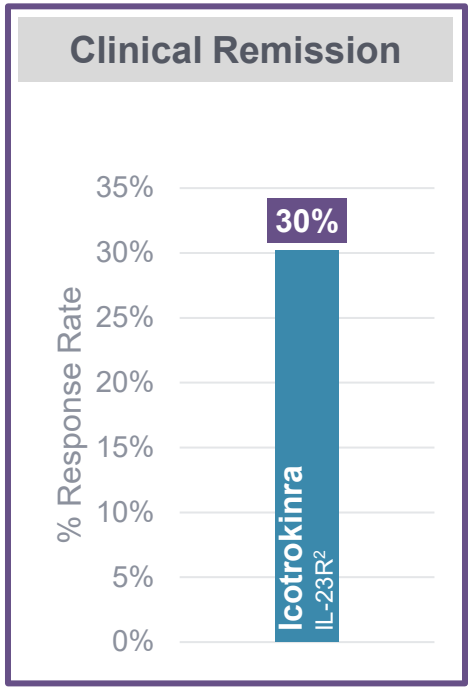
Setting	2025	2026	2027	2028
Plaque Psoriasis	ICONIC Ph3: LEAD, TOTAL, ADVANCE 1 & 2 ✓	★ Mar ’26 ICOTYDE US Approval & Launch ★ Aug ’26 China (NMPA) Approval ★ Sept ’26 EC Approval/Marketing Authorization ✓		
Psoriatic Arthritis	**ICONIC-PsA 1** Ph3, n=552, biologic-naive active ✓ **ICONIC-PsA 2** Ph3, n=813, biologic exposed	Feb ’27*		
Ulcerative Colitis		**ICONIC-UC** Ph3, n=896, in ulcerative colitis	Jan ’28*	
Crohn’s Disease		**ICONIC-CD** Ph 2/3, n~1092, in Crohn’s disease	Sep ’28*	

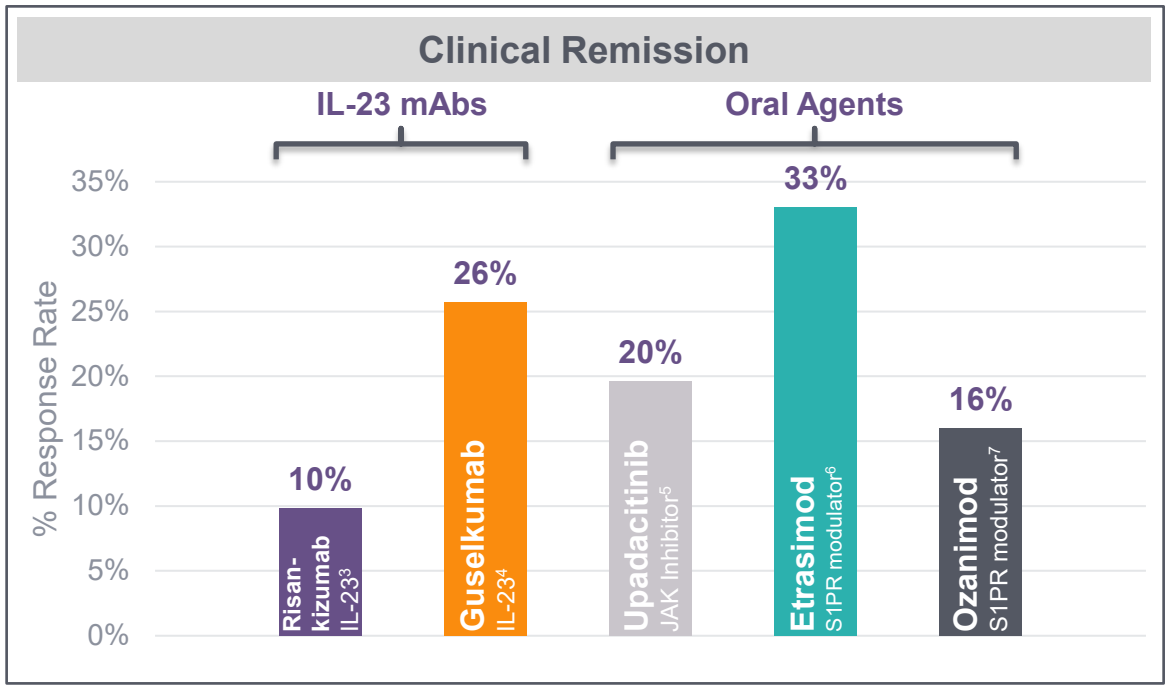
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EC, European Commission.
*Primary Completion Date on clinicaltrials.gov

Icotrokinra Cross-Trial Comparison to Phase 2 Benchmarks in UC[1]

Clinical Remission





Agent	Endpoint Timeframe	Placebo Remission (%)
Icotrokinra	**Wk 12**	**11.1**
Risankizumab	Wk 12	1.7
Guselkumab	Wk 12	9.5
Upadacitinib	Wk 8	0
Etrasimod	Wk 12	8.1
Ozanimod	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. Risankizumab 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. Guselkumab 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*. 2023;165:1443-57.
5. Upadacitinib 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. Etrasimod 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. Ozanimod 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;374:1754-62.

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NOT INTENDED TO COMPARE - CLINICAL COMPARISONS CANNOT BE MADE IN THE ABSENCE OF HEAD-TO-HEAD CLINICAL STUDIES

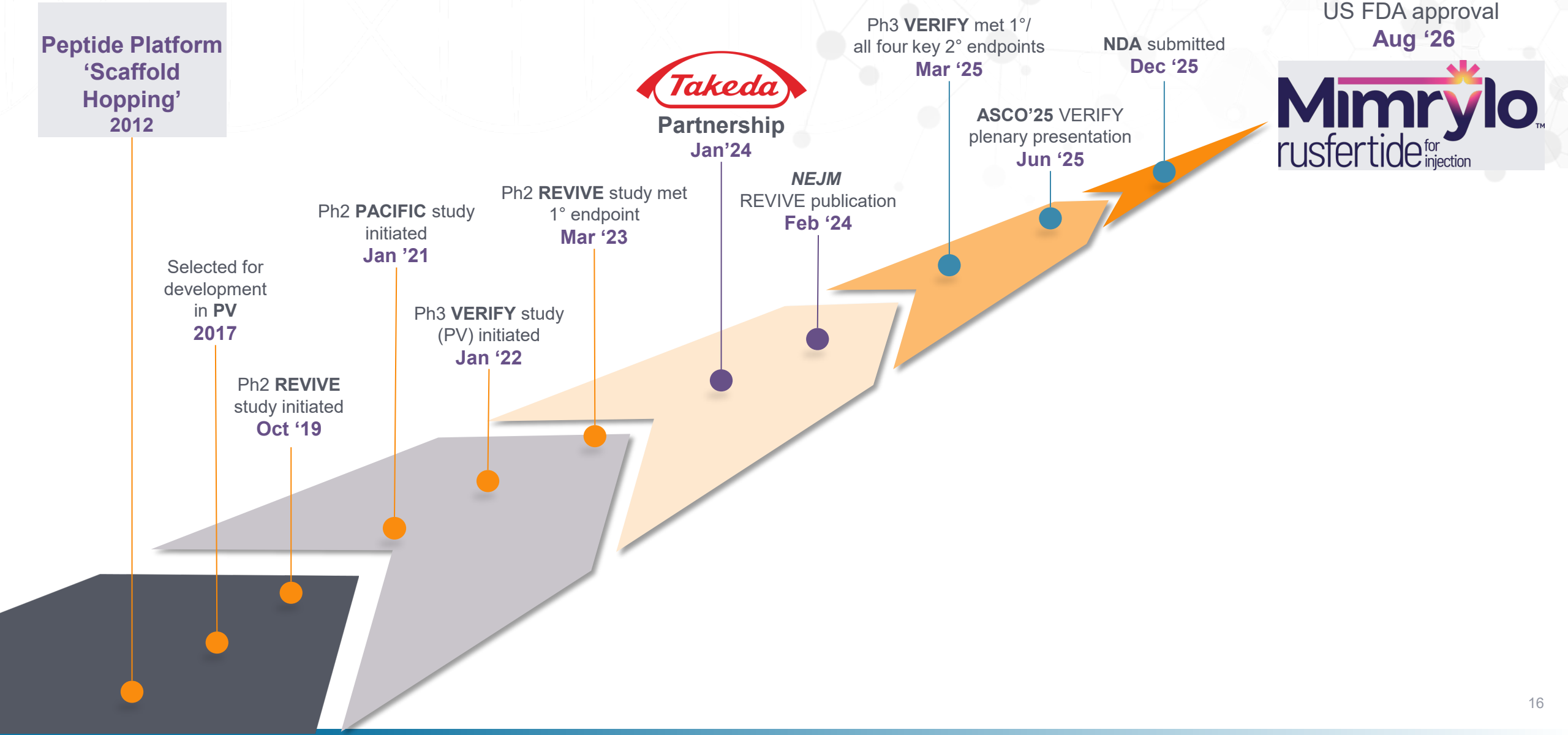
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MIMRYLO™ (Rusfertide): Treatment For Erythrocytosis in Adults With Polycythemia Vera (PV)



MIMRYLO™ (Rusfertide, PTG-300): A Hepcidin Mimetic

Journey from 'Concept to Commercial'



Now FDA Approved: MIMRYLO™

First and Only Hepcidin Mimetic

Mimrylo™ rusfertide for injection

Indication

- Indicated for treatment of erythrocytosis in adults with polycythemia vera (PV)

Polycythemia Vera

- Blood cancer characterized by excessive production of red blood cells[1]
  - Elevated hematocrit (Hct)[2]
  - Primary treatment goal: maintain Hct <45%[3,4]

1. NORD Rare Disease Database, Polycythemia Vera. https://rarediseases.org/rare-diseases/polycythemia-vera/; 2. Spivak JL. *Curr Treat Options Oncol.* 2018;19(2):12; 3. Marchioli R, et al. *N Engl J Med.* 2013; 368(1):22-33; 4. Barbui, T, et al. *Leukemia.* 2018;32(5):1057-69.

MIMRYLO and the MIMRYLO logo are trademarks of Takeda Pharmaceuticals U.S.A., Inc.

MIMRYLO™: Highlights of Prescribing Information (Link)[1]

- **Efficacy:** 76.9% of patients achieved response between Weeks 20-32
  - MIMRYLO maintains hematocrit control and reduces phlebotomy burden

- **Patient reported outcomes (PRO): MIMRYLO improves fatigue in adults with PV**
  - Measured by the PROMIS Fatigue Short Form 8a

- **Safety:** no black box warning
  - **Carcinogenicity:** Rusfertide was not carcinogenic in a 6-month transgenic mouse study at subcutaneous doses up to 25 mg/kg/week or in a 2-year rat carcinogenicity study at doses up to 3 mg/kg/week.
  - **Warnings and Precautions:** New or worsening thrombocytosis, injection-site reactions, and embryo-fetal toxicity.
  - **Adverse reactions:** The most common (>15%) adverse reactions were injection site reactions (56%) and anemia (16%).
  - **Discontinuations:** Adverse reactions which resulted in permanent discontinuation of MIMRYLO included injection site reactions in 2 (0.7%) patients, thrombocytosis in 2 (0.7%) patients, and anemia in 1 (0.4%) patient.

Protagonist Therapeutics

1. MIMRYLO™ (rusfertide). Prescribing information. Takeda Pharmaceuticals America, Inc.; 2026. Accessed on 28 August 2026. https://assets-dam.takeda.com/image/upload/v1787954309/Oncology/News/approval-mimrylo/MIMRYLO_NDA_Approved_Labels.pdf

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 Hct**[1]

2. Patients

- Up to **78% of patients have uncontrolled Hct** ≥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

MIMRYLO™, a hepcidin mimetic, provides an erythrocytosis-specific treatment 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.

MIMRYLO™: Erythrocytosis-Specific Treatment Option for Adults With PV

Peak Revenue Potential of $1-2 Billion[4]

~155k
prevalence[1]
~78k
treated patients with PV in US[2]

Treatment Paradigm

Patients will cycle through various treatments[2]

~41k Phlebotomy (PHL) — And/Or — **~26k** Hydroxyurea (HU) — And/Or — **~6k** Ruxolitinib — And/Or — **~3k** Ropeg-interferon

- Unmet need exists at each step of the treatment landscape
  - **~78% with uncontrolled Hct>45% despite current treatments[3]**
    - **MIMRYLO expected to be used at each step[4]**

MIMRYLO maintains hematocrit control, reduces phlebotomy burden and improves fatigue

1. Mehta J, et al. *Leuk Lymphoma*. 2014;55(3):595-600.
2. Komodo Health closed claims dataset (2016-2023).
3. Verstovsek S, et al. *Ann Hematol*. 2023;102(3):571-81.
4. Takeda 44th Annual J.P. Morgan Healthcare Conference corporate presentation 2026.

Protagonist Therapeutics

MIMRYLO™ (rusfertide) Continues to Be Well Received

- Highlights from Q3'26 Takeda earnings call[1]:

"We are thrilled about the early progress with MIMRYLO."

"The prescribing label allows physicians to use MIMRYLO at any point in the treatment paradigm with no box warning, giving us clear differentiation over other advanced therapies approved in this area."

"Following its late August approval, MIMRYLO was rapidly incorporated into the NCCN guidelines in September, as the only Category 1 option for both low and high-risk PV. Category 1 is reserved for medicine supported by high level Phase 3 evidence and uniform expert consensus."

"The reception from the HCP market and from patients has been…very excited, very positive. Execution of the launch is going very well. It is early days, so we don't have quantitative measures to share."

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1. Takeda Q3 earnings call, October 29, 2026.

MIMRYLO™ (rusfertide) Continues to Be Well Received

- Select quotes from publications:

"*Rusfertide is the first of a novel class of agents targeting the hepcidin regulatory axis. Following its approval, it may become part of the therapeutic armamentarium for selected patients*."[1]

"*Rusfertide represents a novel therapeutic approach to PV by controlling erythrocytosis through restriction of iron availability. Phase 2 and phase 3 studies have demonstrated durable hematocrit control and substantial reductions in phlebotomy requirements, together with improvement in iron deficiency-related parameters*."[1]

"*One of the most clinically relevant observations from VERIFY is the improvement in fatigue. Fatigue remains one of the commonest and most disabling symptoms experienced by patients with PV*."[2]

"*By validating iron homeostasis as a therapeutic target, the study expands treatment options beyond conventional phlebotomy and supports a more personalized approach that balances disease control, treatment burden, and patient priorities*."[2]

"*VERIFY not only introduces a new treatment but also validates iron homeostasis as a therapeutic target at precisely the moment that the field is redefining what successful treatment in PV should look like*."[2]

1. Vannucchi AM, et al. Rusfertide for the Treatment of Polycythemia Vera. *Expert Opin Pharmacother.* 2026; Epub ahead of print.
2. Torre E and Harrison C. Beyond Phlebotomy: Iron Homeostasis in the Next Phase of Polycythemia Vera Management. *J Clin Oncol.* 2026;Epub ahead of print.

Protagonist Therapeutics

R&D Pipeline
I&I, Hematology, Obesity

PN-881: A Potential Best-in-Class Oral IL-17A and IL-17F Antagonist

Clinically and commercially validated target for multiple inflammatory conditions



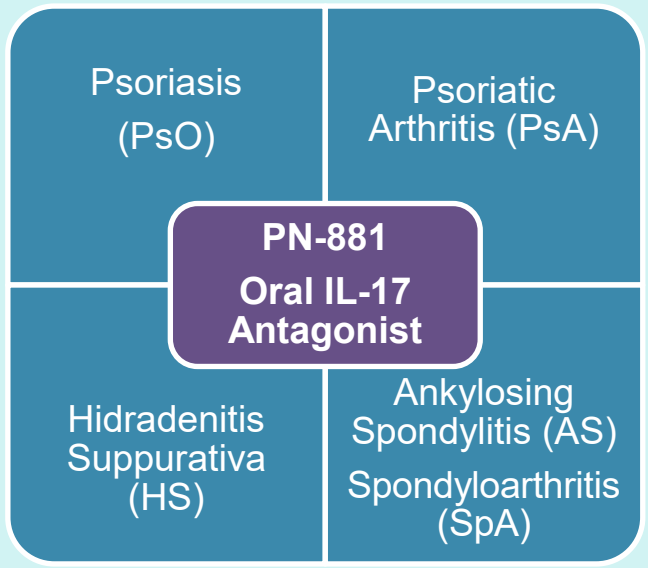
Targeting a $55B+ Market Opportunity with Differentiated ORAL IL-17 Inhibition

PN-881: A Potential Best-in-Class Oral IL-17A and IL-17F Antagonist

IL-17: Large & Expanding Market Opportunity

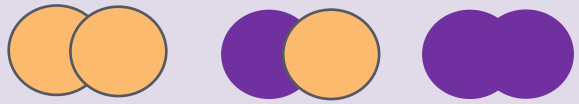
$12B	CURRENT IL-17 SALES[1]
28%	ANNUAL MARKET GROWTH[2]
~2.5M	PATIENTS ELIGIBLE BUT UNTREATED[3]
>$55B	LONG-TERM MARKET OPPORTUNITY[4]

Strategic Indication Expansion



PN-881: Differentiated Target Product Profile

PN-881 Blocks All Three IL-17 Dimers



- ***Oral Peptide***
- ***Triple specificity***[5] matching Bimzelx profile
- Potential ***best-in-class profile***

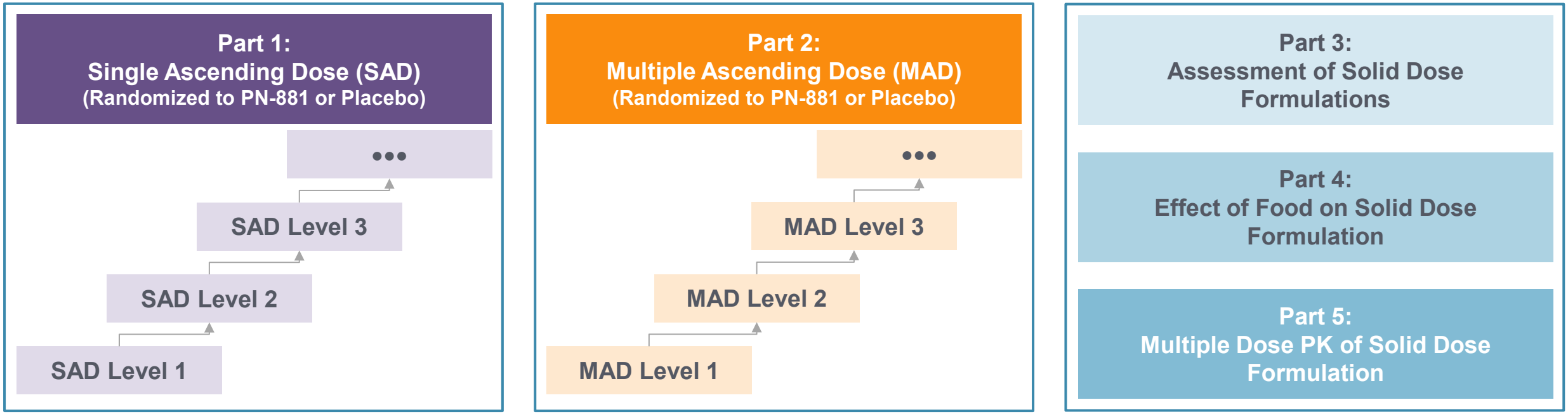
PN-881: A wholly-owned **ORAL** IL-17A and F antagonist in Clinical Studies

1. 2025 Company reported revenues (Novartis, Eli Lilly, UCB)
2. Historical CAGR based on FY2023-2025 actual reported revenues (Novartis, Eli Lilly, UCB)
3. Clarivate (PsO, PsA, AxSpA) and DelveInsight (HS), 2025 diagnosed and treated prevalence in G7 markets. Untreated patients calculated as moderate-to-severe diagnosed population minus drug-treated population
4. 2032 projected market size for PsO, PsA, axSpA, and HS; Evaluate Pharma
5. Reich et al., *N Engl J Med* 2021;385:142-52.

Protagonist Therapeutics

PN-881: Comprehensive Phase 1 Study in Healthy Volunteers (N~142)

Phase 1 Study Completed



- **Primary endpoint:**
  - Incidence and severity of treatment-emergent adverse events (pre-dose to 7 days after last dose)
- **Secondary endpoint:**
  - Pharmacokinetics

Protagonist Therapeutics

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

	Neonatal Human Dermal Fibroblast					
	IL-17AA[1]		IL-17FF[1]		IL-17AA+IL-17FF[2]	
	IC_{50} (nM)	IC_{90} (nM)	IC_{50} (nM)	IC_{90} (nM)	IC_{50} (nM)	IC_{90} (nM)
Oral Peptide, PN-881	**0.0026**	**0.031**	**0.015**	**0.124**	**0.013**	**0.098**
Injectable mAb, Bimzelx® (Bimekizumab)	0.0007	0.003	0.014	0.037	0.015	0.071

mAb, monoclonal antibody; PsO, psoriasis.

[1]IC_{50}/IC_{90} values reflect drug potency for inhibiting IL-17 signaling at IL-17 levels relevant for PsO patients, i.e., IL-17A = 0.1 ng/mL; IL-17F concentration = 1 ng/mL

[2]IL-17A and IL-17F were used in vitro in a PsO-relevant ratio of 1:30, i.e., 0.1 ng/mL IL-17A + 3 ng/mL IL-17F, to demonstrate the inhibitory potential of PN-881 compared to bimekizumab.

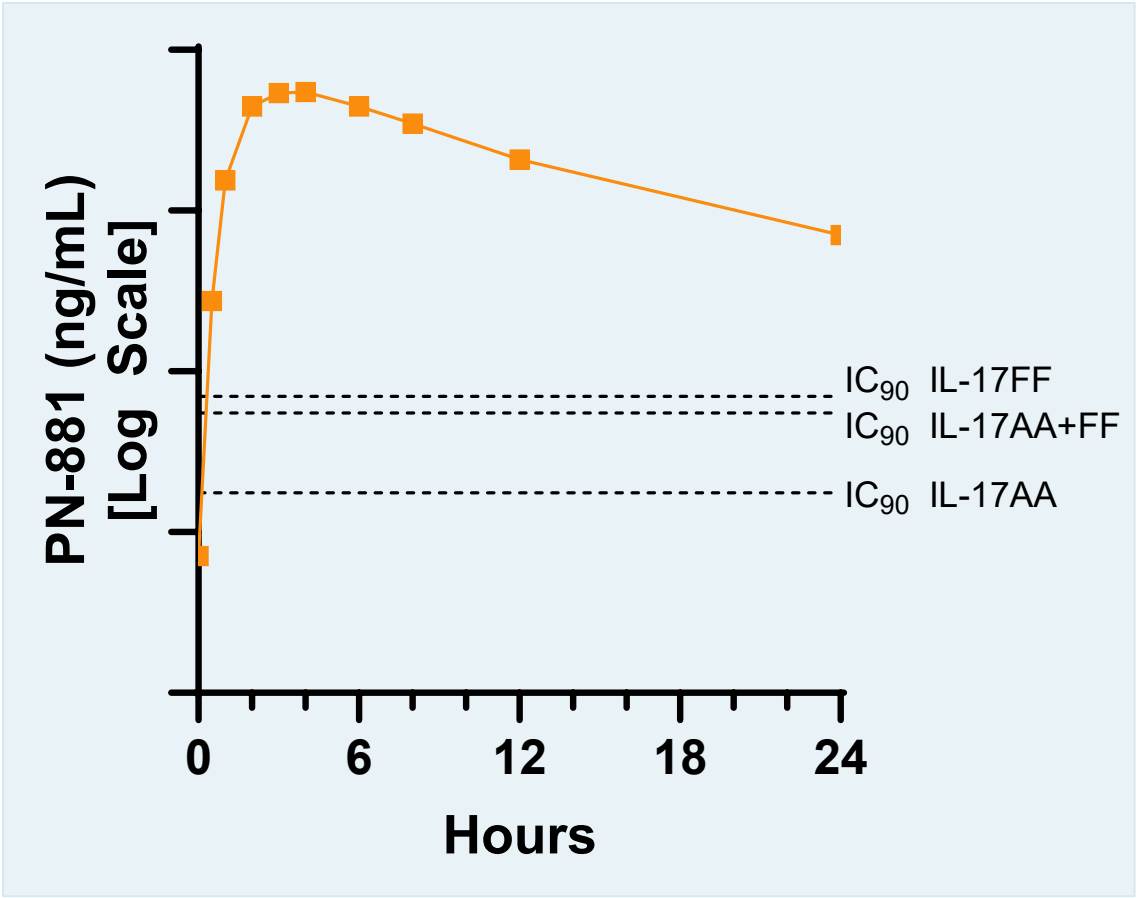
Protagonist Therapeutics

Data on File. Protagonist Therapeutics, Inc.

PN-881: Phase 1 Study

Pharmacokinetic Results Support a Comprehensive Phase 2b Study in Plaque Psoriasis

- **Achieved 24-hour C_{trough} levels significantly higher than prospectively targeted IC_{90} (IL-17AA, IL-17FF, IL-17AA+FF) values with once-daily oral dosing**
- **Drug accumulation results in higher drug levels at steady state** (data not shown)
- Generally well tolerated; no serious adverse events
- Phase 1 data to be presented at a future medical meeting
- Phase 2b dose range-finding study in plaque psoriasis to be initiated in early Q1 2027

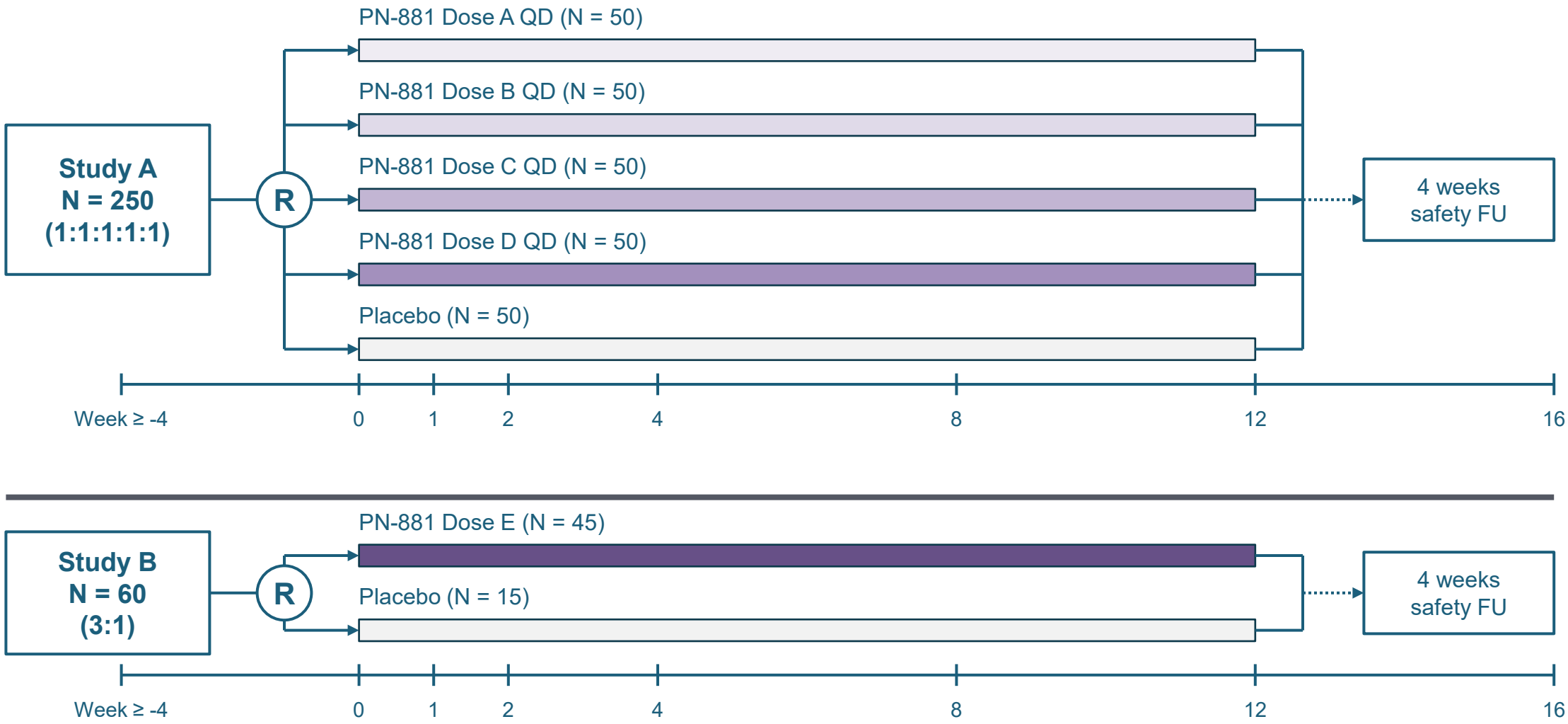


PN-881 Plasma Concentrations Several Fold Higher Than IC_{90} Values For Both Isoforms (AA & FF) and IL-17AA+FF

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PN-881: Comprehensive Phase 2b RESOLVE-PsO Study Design

Study initiation ~Q1’27



Primary Endpoint: PASI 75 at Week 12

Protagonist Therapeutics

PN-881: Successful Ph1 Lays a Strong Foundation for Comprehensive Ph2b Program

Clinical Development Plans in Psoriasis and Other Potential Indications

PN-881 Oral IL-17 Antagonist

2H 2026	1H 2027	2H 2027	1H 2028
➢ Ph1 completion	➢ Ph2b PsO study initiation (early Q1 '27) ➢ Ph1 topline	➢ Ph2b PsO enrollment completion ➢ Evaluation of potential additional Ph2 study (e.g., PsA, HS)	➢ Potential second Ph2 study initiation (e.g., PsA, HS) ➢ Ph2b PsO topline

HS, hidradenitis suppurativa; PsO, plaque psoriasis.

Protagonist Therapeutics

PN-8047: An Oral Hepcidin Functional Mimetic

Working towards a hepcidin pathway based ORAL option in polycythemia vera



PN-8047: Oral Hepcidin Functional Mimetic

Leveraging Our Expertise in the Hepcidin Pathway

- Rusfertide established hepcidin mimetics as a therapeutic option for polycythemia vera
  - Clinical validation of hepcidin biology

- **PN-8047:** Builds on Protagonist's knowledge base of hepcidin pathway
  - **Novel oral small molecule**; selected from extensive head-to-head comparison of different modalities
  - Potentially maximizes the total addressable global market for hepcidin mimetics
  - Provides a therapeutic option that may reduce treatment barriers

- Wholly-owned asset

Protagonist Therapeutics

PN-8047: An Oral Hepcidin Functional Mimetic for Targeting Polycythemia Vera

PN-8047 has similar potency as rusfertide and is superior to hepcidin

	Human-FPN Potency EC_{50} (nM)
Hepcidin	13.7
Rusfertide	2.5
PN-8047	**4.3**

Table shows average values for effective concentration for 50% signal (EC_{50}) in nano-molar (nM)
Human-FPN assay measured functional response of increases in transferrin-receptor1 due to increase in intracellular iron concentrations after ferroportin internalization
Cyno-FPN assay measured reduction in NanoLuc® Luciferase signal, downstream of ferroportin internalization

FPN, Ferroportin; Cyno, Cynomolgus Monkey

Protagonist Therapeutics

PN-8047: Novel Potent Oral Small Molecule With Excellent PK, PD, and Efficacy Properties

Attributes	Summary of PN-8047 Properties
Potency	✓ Nanomolar potency in the T47D-TfR1 functional assay ✓ Similar potency as Rusfertide
in vitro ADME	✓ Metabolically stable in liver microsomal incubations ✓ Good permeability for oral dose
PK	✓ Oral exposure and $T_{1/2}$ in rodents, cyno, and dog sufficient for oral daily dosing
PD Model	✓ Iron reduction after single and repeat oral dosing to dog and monkey to support once-daily oral dosing ✓ Sustained iron reduction for 16 hr
Efficacy Model	✓ Efficacy in the erythropoietin (EPO)-induced mouse model for erythrocytosis ✓ Reduction of hemoglobin and hematocrit after repeat oral dosing to cynos
DDI	✓ No DDI risk potential
Safety	✓ No major off-target activities ✓ Tolerated in 7-day rat MTD

Phase 1 initiation in Q1 ’27
PD-based clinical PoC achievable in phase 1

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PN-8047: Oral Hepcidin Functional Mimetic Development Timelines



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Metabolic Pipeline: Addressing the Need For Unimolecular Oral Anti-Obesity Therapies

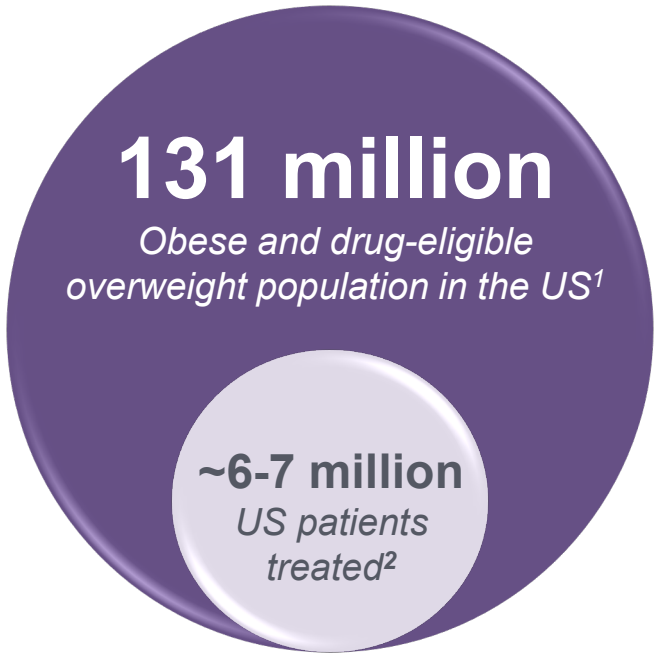
Triple-G, Dual-G, and AmylinR Agonists



Obesity: Unprecedented Pharmaceutical Opportunity in the US and Worldwide

Only ~5% of Eligible Patients Receive Drug Treatment[1]

Massive Untapped Opportunity in Obesity Care



- Obesity is a global epidemic
  - In 2024, nearly ***40% of Americans were obese*** or considered drug-eligible overweight[3]
- Low Treatment Penetration
  - Only ~5% of eligible patients receive drug treatment[1]
- Current challenges with anti-obesity drugs
  - Successful maintenance, as ~70% of patients discontinue treatment within 1 year[4]
  - Convenience; needle avoidance
  - Early days & limited options
  - Adverse effects

‘Oral’ and ‘more effective’ agents:
An attractive option for a chronic condition and affiliated co-morbidities

Protagonist Therapeutics

[1] Clarivate Disease Landscape & Forecast – Obesity/Overweight (November 2025); Drug-eligible Population: obese (BMI≥30) and drug-eligible overweight (27≤BMI<30 with at least one weight-related comorbidity); [2]Morgan Stanley Research, May 2026; Bernstein Research, May 2026; [3]HSBC Research, Dec 2025. [4]MagellanRx Research July 2024

Four of the Current Top 10 Best-Selling Drugs are Peptide-Based Therapies[1]

2015

1 peptide branded therapy in top 10

Humira	$14.0B	mAb
Harvoni	$13.9B	SM
Enbrel	$8.7B	Fusion
Remicade	$8.4B	mAb
Rituxan	$7.1B	mAb
Lantus	$7.0B	Peptide
Avastin	$6.8B	mAb
Herceptin	$6.6B	mAb
Revlimid	$5.8B	SM
Sovaldi	$5.3B	SM

→

2025

4 peptide branded therapies in top 10

Keytruda	$31.7B	mAb
Mounjaro	$23.0B	Peptide
Ozempic	$19.2B	Peptide
Dupixent	$17.7B	mAb
Skyrizi	$17.6B	mAb
Eliquis	$14.4B	SM
Darzalex	$14.4B	mAb
Biktarvy	$14.3B	SM
Zepbound	$13.5B	Peptide
Wegovy	$12.0B	Peptide

1 → 4
Peptides among the top 10

$7B → $68B
Combined top-10 peptide sales

~10×
Growth over the decade

Protagonist Therapeutics

1. Evaluate. World preview 2026: Big drugs. Bigger questions. Evaluate. Published June 23, 2026. Accessed August 3, 2026. Accessed at: https://www.evaluate.com/thought-leadership/world-preview-2026/. Company Annual Reports. 2025/2026.

PN-477o: A Novel Triple GLP-1/GIP/GCG Receptor Agonist Oral Peptide

Potential Improvements

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

ORAL Triple-Agonist Once-daily Dosing

PN-477o

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GCG, Glucagon; GIP, Glucose-Dependent Insulinotropic; GLP-1, Glucagon-Like Peptide-1.

PN-477o: Triple Agonist (GLP-1R, GIPR, GCGR) Oral Peptide

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
in vivo Pharmacodynamics / Efficacy Model	✓ Potent weight loss in normal NHPs and normal beagle dogs ✓ Excellent efficacy in mouse diet-induced obesity (DIO) model ✓ Glycemic control demonstrated by a glucose tolerance test
in vivo Pharmacokinetics	✓ Oral bioavailability demonstrated in mouse, rat, dog, cynomolgus monkey ✓ GI stability and oral PK supports once-a-day oral dosing ✓ PK profile supports once-a-week subcutaneous dosing

GI: Gastrointestinal; PK: Pharmacokinetic

PN-477 is a Novel, Potent Triple-G Agonist Peptide

	Human EC_{50} (nM)				
	GLP-1R		GIPR		GCGR
Tirzepatide[1,‡] (Eli Lilly **Dual** GLP-1R/GIPR)	23.1	14x	1.7		NA[†]
Retatrutide[2,‡] (Eli Lilly **Triple** GLP-1R/GIPR/GCGR)	14.6	9x	1.6		19.2
PN-477	6.4	16x	0.4		14.8

- More potent than retatrutide for GLP-1R and GIPR

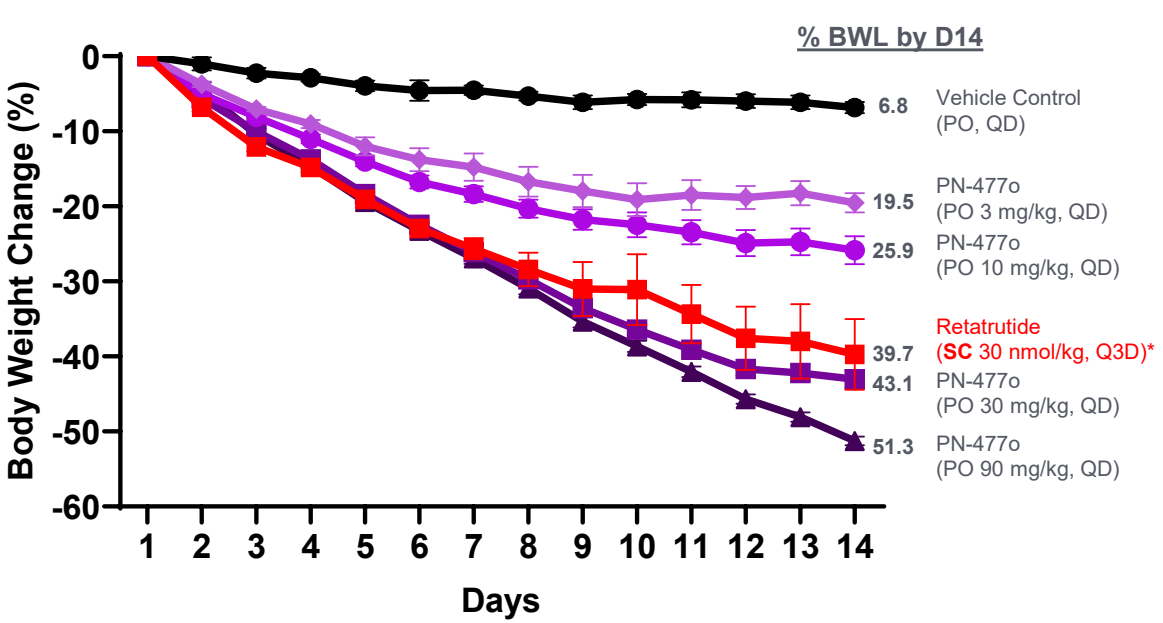
Protagonist Therapeutics

[1] Coskun T, Mol Metab 2018; [2] Coskun T, Cell Metab 2022
‡*1PlusChem Cat. 1P01MVTY (Tirzepatide); MCE Cat. HY-P3506 (Retatrutide)*

PN-477 Promotes Significant Body Weight Loss

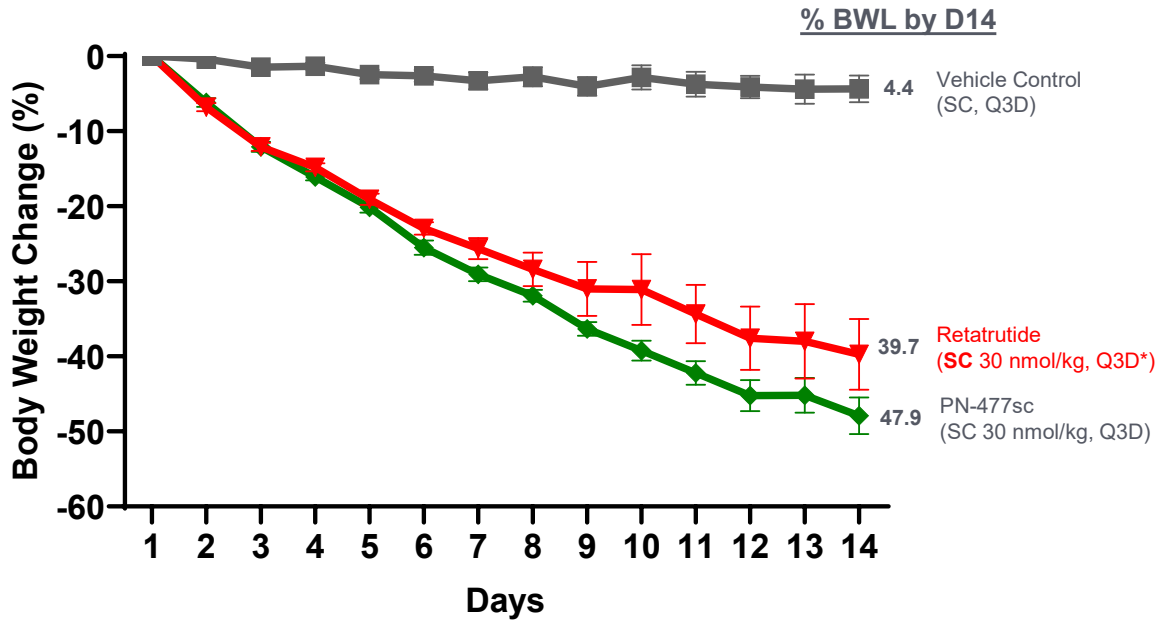
Pre-Clinical Efficacy Study Using DIO Mice

% Body Weight Change, PO: Days 1-14



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

% Body Weight Change, SC: Days 1-14



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

Protagonist Therapeutics

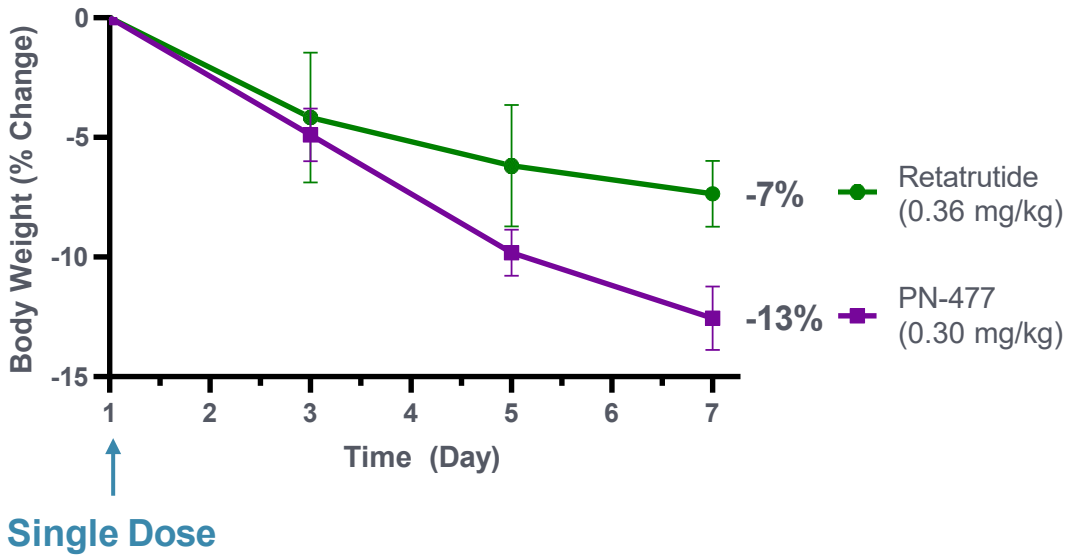
BWL: Body Weight Loss; DIO: Diet Induced Obese; PO, per os (oral); SC, subcutaneous, QD, once a day; Q3D, every 3 days.

Data points depict mean ± SEM.

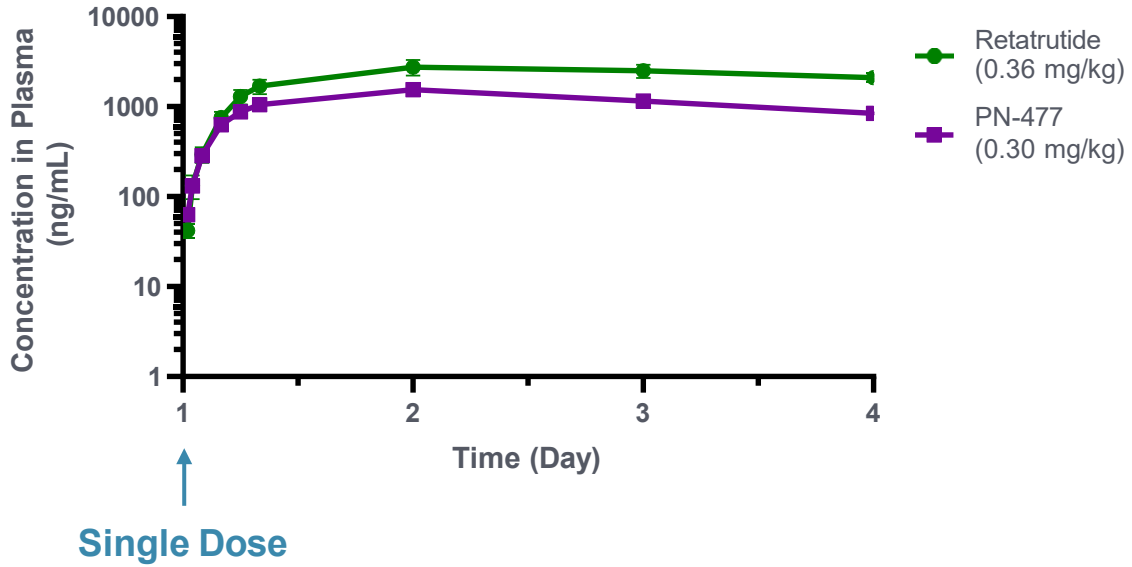
*Retatrutide SC 30 nmol/kg dose is the highest dose reported for DIO mouse efficacy study (Cell Metabolism 34, 1234–1247, September 6, 2022).

Single SC Dose PN-477 Body Weight Loss Study In Normal Cynomolgus Monkeys

% BW Change, SC



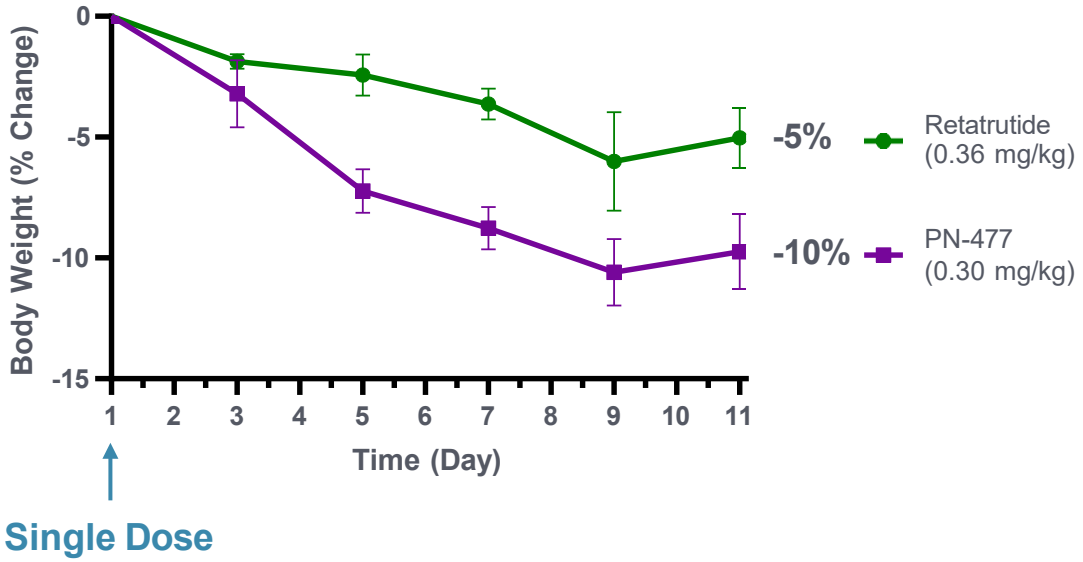
PK, SC



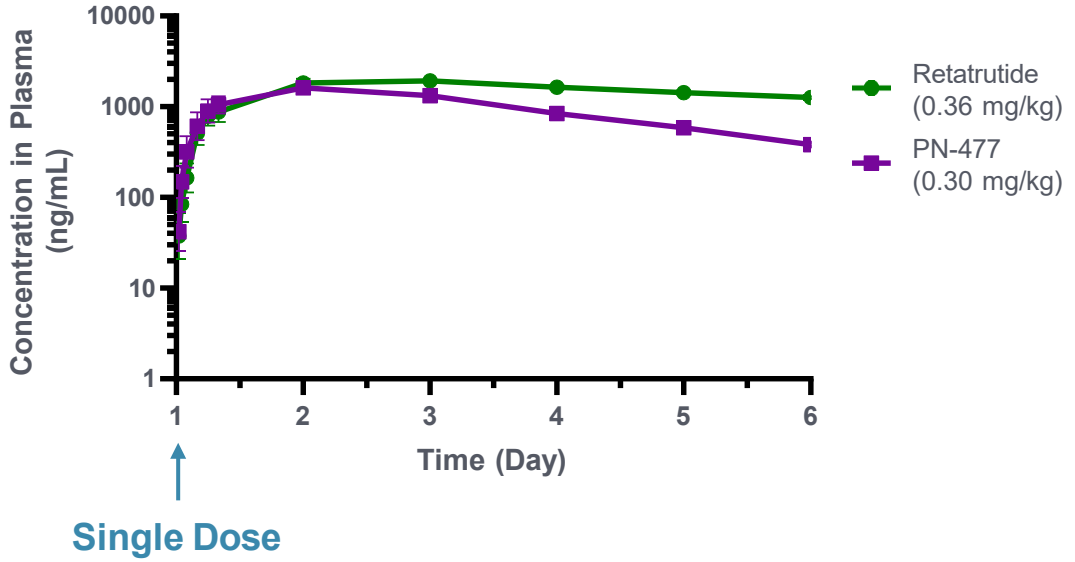
BW, Body Weight; PK, Pharmacokinetics; SC, subcutaneous

Single SC Dose PN-477 Body Weight Loss Study In Normal Beagle Dogs

% BW Change, SC



PK, SC

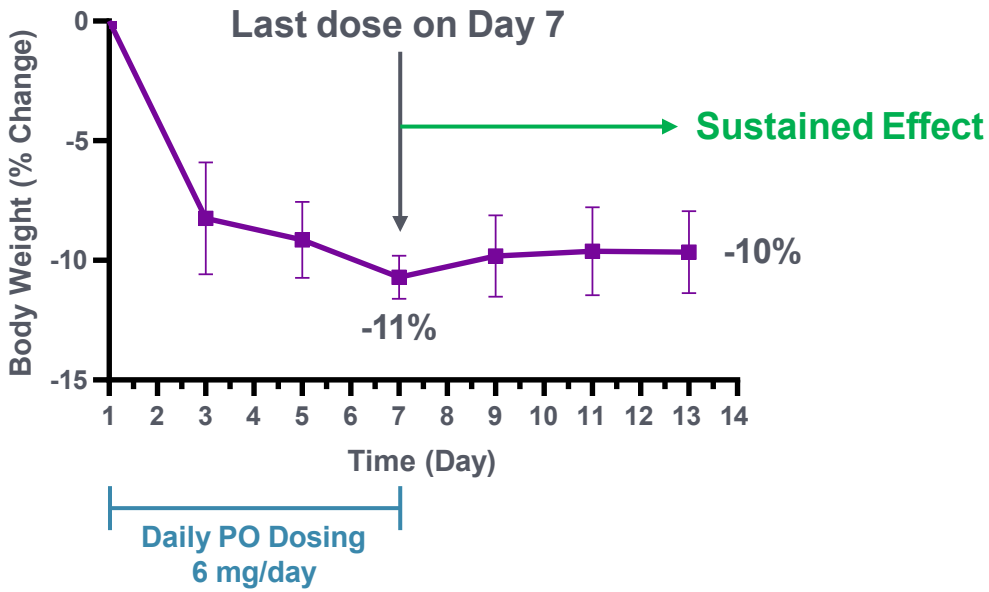


BW, Body Weight; PK, Pharmacokinetics; SC, subcutaneous

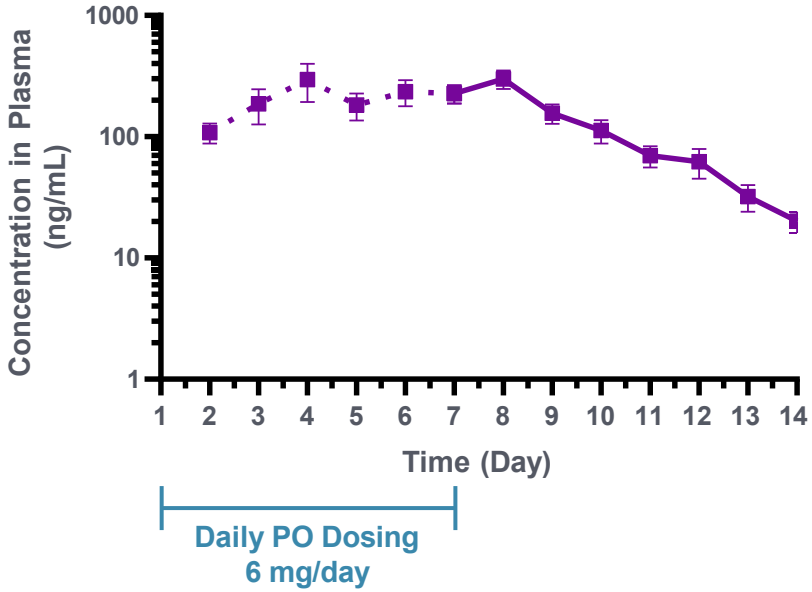
7-Day Oral Dosing PN-477 Body Weight Loss Study In Normal Cynomolgus Monkeys

Weight Loss Sustained for 6 Days After Last Dose

% BW Change, PO



PK C_{trough} Day 1-7, PO



Oral PN-477 PK profile suggests **once-daily human dosing and sustained weight loss**

Protagonist Therapeutics

BW, Body Weight; PO, Per Os (oral); PK, Pharmacokinetics

PN-477sc-01: Phase 1 First-in-Human SAD Study

Preliminary Proof of Clinical Activity Achieved

- Single subcutaneous doses of PN-477sc were tested in overweight and obese volunteers

- Dose-related PK, PD, and clinical effects observed:
  - weight loss
  - insulin & C-peptide secretion
  - HR changes
  - mild/moderate GI effects

- Potency appears to be higher vs. retatrutide based on observation of similar clinical activity at 4- to 5-fold lower doses‡,[1,2]

Based on encouraging positive results from the PN-477sc SAD study, we have prioritized the PN-477o clinical development program

Protagonist Therapeutics

‡ Cross-trial comparison. 1. Coskun T, et al. LY3437943, a novel triple glucagon, GIP, and GLP-1 receptor agonist for glycemic control and weight loss: From discovery to clinical proof of concept. *Cell Metabol*. 2022;34(9):1234-47. 2. Data on File. Protagonist Therapeutics, Inc.

PN-477o: A Potential Best-in-Class Once-Daily Oral Triple Agonist

- Novel, orally stable, and potent triple agonist (GLP-1R, GIPR, and GCGR)
  - Achieved target balance of GLP-1R, GIPR, GCGR potencies (absolute and relative)
- Preclinical PoC:
  - Weight loss and quality of weight loss in DIO mice benchmarks favorably versus retatrutide
  - Weight loss after single dose of PN-477 benchmarks favorably versus retatrutide in normal dogs and cynomolgus monkeys
  - PK profiles support once-daily oral dosing and potentially once-weekly oral dosing in a maintenance phase
- Phase 1 SC SAD Study:
  - **Observed positive dose-related pharmacokinetic, pharmacodynamic and clinical activity**
  - **Based on these highly encouraging findings, Protagonist has made a strategic decision to prioritize the orally administered PN-477o clinical development program**
- Phase 1 oral study: to be initiated in 1H 2027

PN-477o: Near-Term Clinical Development Plan

PN-477o Anti-Obesity

2026	1H 2027	2H 2027
➢ IND-enabling studies	➢ PN-477o Ph1 SAD/MAD (7-day) initiation	➢ PN-477o Ph1b MAD (13 weeks) initiation

PN-458: A Highly Potent Oral Dual GLP-1/GIP Receptor Agonist

Potential Weight Loss Profile and GI Tolerability of Tirzepatide

	Human EC_{50} (nM)		
	GLP-1R	**GIPR**	**GCGR**
Tirzepatide[1,‡] (Eli Lilly **Dual** GLP-1R/GIPR)	23.1	1.7	NA[†]
PN-458	**7.8**	**0.86**	**NA[†]**

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

[†] *NA: Not Active*

- PN-458 has higher potency than tirzepatide for GLP-1R and GIPR

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1. Coskun T, Mol Metab 2018.

PN-458 Dual Agonist (GLP-1R, GIPR) Peptide

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

Attribute	Criteria
Potency	✓ nM potency vs GLP-1R, GIPR
Stability	✓ Stable in simulated gastric and intestinal fluids ✓ Stable in serum ✓ Metabolic stability ✓ Thermostability
Efficacy Model	✓ Efficacy in mouse diet-induced obesity (DIO) model
In vivo Pharmacodynamics	✓ Glucose control demonstrated with glucose tolerance test
In vivo 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

IND-enabling studies in progress

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GI: Gastrointestinal; PK: Pharmacokinetic

Two Anti-Obesity Assets Create Strategic Flexibility

Preclinical Data Support Best-in-Class Potential For Both Programs

PN-477

TRIPLE AGONIST

GLP-1R / GIPR / GCGR agonist peptide

DESIGN GOAL	**Maximize weight loss magnitude and quality (preferential fat mass loss)**
BENCHMARK	**Retatrutide-class profile**
FORMAT	**Once-daily oral**
PRECLINICAL	**Significant body weight loss in DIO mice, dogs, and cynomolgus monkeys**
CLINICAL	**Preliminary PoC achieved in Ph1 SAD SC study; Ph1 oral study initiation 1H 2027**

PN-458

DUAL AGONIST

GLP-1R / GIPR agonist peptide

DESIGN GOAL	**Balance weight loss with GI tolerability**
BENCHMARK	**Tirzepatide-class profile**
FORMAT	**Once-daily oral**
PRECLINICAL	**Significant body weight loss in DIO mice, dogs, and cynomolgus monkeys**
CLINICAL	**Ph1 oral study initiation 2H 2027**

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GCG, glucagon; GI, gastrointestinal; GIP, glucose-dependent insulinotropic polypeptide; GLP-1, glucagon-like peptide-1; R, receptor; SAD, single ascending dose; SC, subcutaneous.

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What's Next?



Protagonist Therapeutics

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

	1H 2026	2H 2026	2027
ICOTYDE® Partner: J&J	★ **ICOTYDE® approved for moderate to severe plaque psoriasis**	❖ **Commercial** ❖ **EC Approval/MA: September 2026**	❖ **Revenues**
MIMRYLO™ Partner: Takeda	❖ NDA accepted; priority review granted ❖ Opted-out	★ **MIMRYLO™ approved for erythrocytosis in PV**	❖ **Revenues**
PN-881*	Oral IL-17 antagonist ❖ Ph1 ongoing	❖ **Ph1 completion ✓**	❖ **Comprehensive Ph2b PsO Initiation (early Q1 '27)** ❖ **Ph1 data** ❖ **Evaluation of potential additional Ph2 study (e.g., PsA, HS)**
PN-477sc* **PN-477o***	Anti-obesity DCs ❖ IND-enabling studies	❖ **PN-477sc Ph1 SAD PoC ✓**	❖ **PN-477o Ph1 SAD (1H '27)** ❖ **PN-477o Ph1b MAD initiation (2H '27)**
PN-8047*	Oral Hepcidin DC ❖ IND-enabling studies	❖ IND-enabling studies (completion anticipated)	❖ Ph1 SAD/MAD initiation ❖ **Ph1 PD PoC (Mid '27)** ❖ **Ph2 PV initiation (2H '27)**
PN-458o*			Dual GLP/GIP DCs ❖ Ph1 SAD initiation (Mid '27) ❖ Ph1 MAD initiation (2H '27)
Discovery*	❖ Oral IL-4Rα antagonist ❖ Amylin oral mono/poly-agonists		

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*Wholly-owned by Protagonist Therapeutics, Inc. DC, Development candidate, ready for IND-enabling studies; EC, European Commission; IND, investigational new drug; MA, Marketing Authorization; MAD, multiple ascending dose; NDA, new drug application; PD, pharmacodynamic; PoC, proof of concept; PsO, psoriasis; SAD, single ascending dose. ICOTYDE is a registered trademark of Johnson & Johnson and its affiliates.

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Thank you

