Protagonist Therapeutics

COMPANY OVERVIEW

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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 J&J and Takeda; market acceptance ICOTYDE™ (icotrokinra); the timing and results of ICOTYDE clinical trials; the commercial potential of rusfertide and other product candidates; our plans for future capital allocation; timing and results related to our pre-clinical and clinical product candidates (including PN-881, PN-477, PN-458 and PN-8047, among others); actions of the U.S. Food and Drug Administration ("FDA") and foreign regulatory agencies, including expectations regarding timing of FDA approval of the NDA for rusfertide; 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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Protagonist Therapeutics: Revenue Engine and Pipeline

Revenue Engine

Commercial & Partnered

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

FDA Approved: Mar ’26
EMA CHMP Positive Opinion: Jul ’26
Moderate-to-Severe Plaque Psoriasis

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

Rusfertide
SC Hepcidin Mimetic • Partner: Takeda

PDUFA: Aug ’26
Potential Indication: Polycythemia Vera

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

Wholly-Owned Pipeline

Inflammation & Immunology

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

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

Metabolic

Oral & SC PN-477 · GLP/GIP/GCG
SC Ph1 ongoing; 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

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1. HSBC Dec 2025 Consensus Forecast (across all indications); 2. Takeda 44th Annual J.P. Morgan Healthcare Conference corporate presentation 2026.
ICOTYDE is a trademark of Johnson & Johnson and its affiliates.

Protagonist Partnership Economics

Expected to Finance Our R&D Pipeline and Potential Capital Return

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

$387.5M	$580M	6–10%	>$10B[1]
Payments received	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 · EMA CHMP positive opinion: Jul ’26

7.25% weighted-avg royalty at $4B; 10% for annual sales ≥$4B

Rusfertide; SC Hepcidin Mimetic; Partner: Takeda

$525M	$1.05B	14–29%	$1–2B[2]
Payments received	Future milestones	Tiered worldwide royalties	Takeda-guided peak sales

FDA Priority Review; PDUFA: Aug ’26 · Ph3 VERIFY PV study met primary + all 4 key secondary endpoints

21% weighted-avg royalty at $1.5B; 29% for annual sales ≥$1.5B

$912.5M in upfront and milestone payments earned through June 2026

Protagonist Therapeutics

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

Expected to Finance Our R&D Pipeline and Potential Capital Return

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

- **6%-10% tiered royalties**
  - 7.25% weighted average at $4B annual sales
  - 10% for annual sales ≥$4B
  - $425M sales milestones with highest hurdle at $5 billion annual net sales

Illustrative royalties in peak sales year				
Annual net sales*	$5.0B	$10.0B	$15.0B	$20.0B
Pre-tax royalty receivable*	$0.4B	$0.9B	$1.4B	$1.9B

Rusfertide; SC Hepcidin Mimetic; Partner: Takeda

- **14%-29% tiered royalties**
  - 21% weighted average at $1.5B annual sales
  - 29% for annual sales ≥$1.5B
  - $775M sales milestones with highest hurdle at $2.5 billion annual net sales

Illustrative royalties during peak sales year				
Annual net sales*	$1.0B	$1.5B	$2.5B	$3.5B
Pre-tax royalty receivable*	$0.2B	$0.3B	$0.6B	$0.9B

Significant royalties and up to $1.63B in future milestone payments

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* Sensitivity analysis purposes only and does not represent management guidance, expectations or projections
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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
Rusfertide Hepcidin mimetic	Hematology	**FDA review (NDA for PV)**	FDA decision (PDUFA: Aug ’26)
PN-881 Oral IL-17A/F	I&I	**Ph1; Ph2b PsO**	Ph1 safety/PK completion Ph2b PsO dose finding/PoC
PN-477 Triple agonist; oral + SC	Metabolic	**Ph1 SC and Oral**	Ph1 SC SAD/Ph1b MAD (13 weeks) PoC Ph1 Oral SAD/MAD (7-day) Ph1b Oral MAD (13 weeks) PoC
PN-458 Dual agonist; oral	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 market >$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 and Late-Stage Assets**
  - ICOTYDE
  - Rusfertide
- **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, rusfertide)
- **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**
  - $849.5M cash (2Q26); additional opt-out, milestones, and royalty payments expected by year-end
  - Royalty streams from ICOTYDE (6–10%) and rusfertide (14–29%), plus milestone payments
  - No expected equity raise in the foreseeable future
  - Potential share buyback program announcement by year-end

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

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

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.

Protagonist Therapeutics

ICOTYDE™ (icotrokinra)

US FDA approval of ICOTYDE™, formerly PN-235

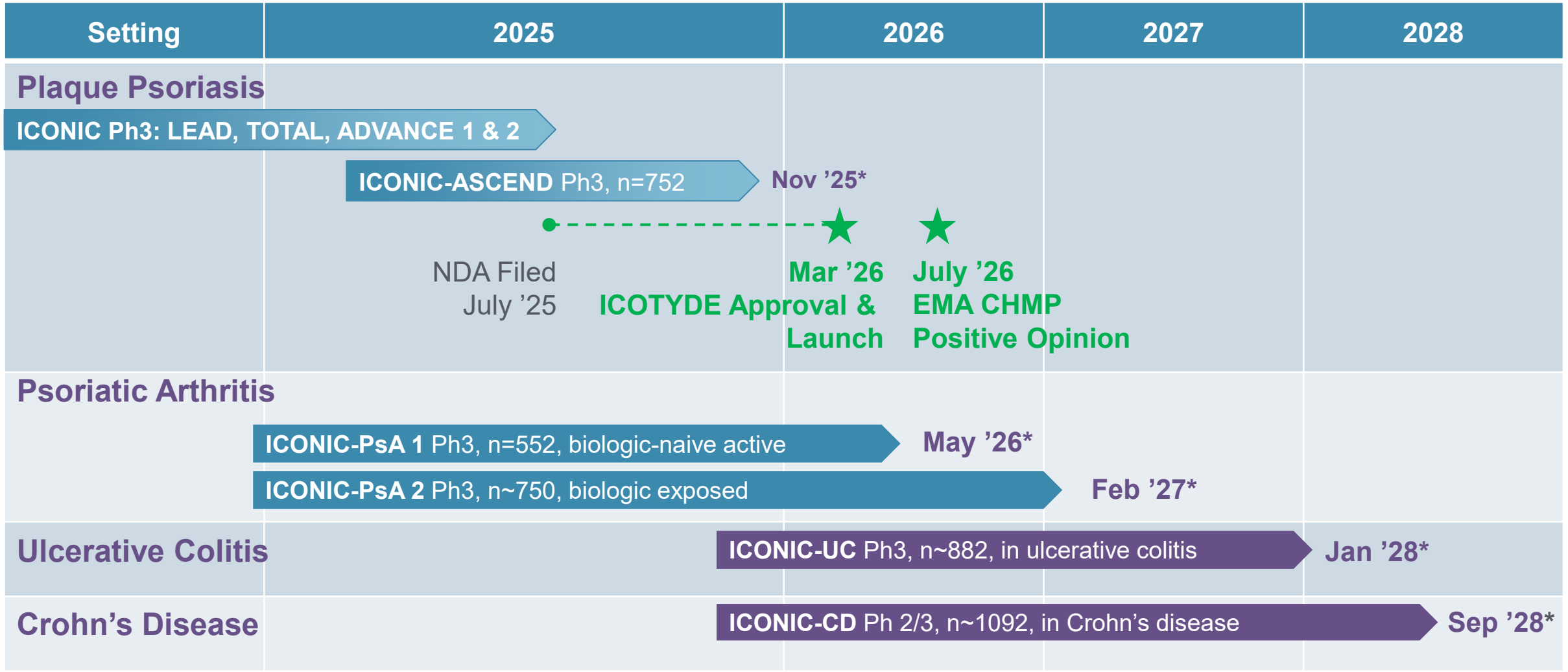
- Johnson & Johnson partnership overview
  - 2017 to present
  - Protagonist completed pre-clinical and first Ph1 study[1]
  - J&J responsible for further development and commercialization

- ICOTYDE is the first and only IL-23R targeted oral peptide to
  - clear skin for moderate to severe plaque psoriasis patients, 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.

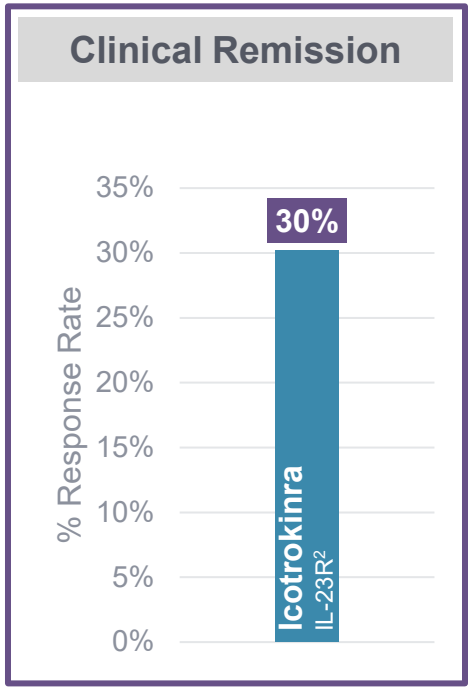
Icotrokinra Potential Expansion of Multiple Indications in Coming Years

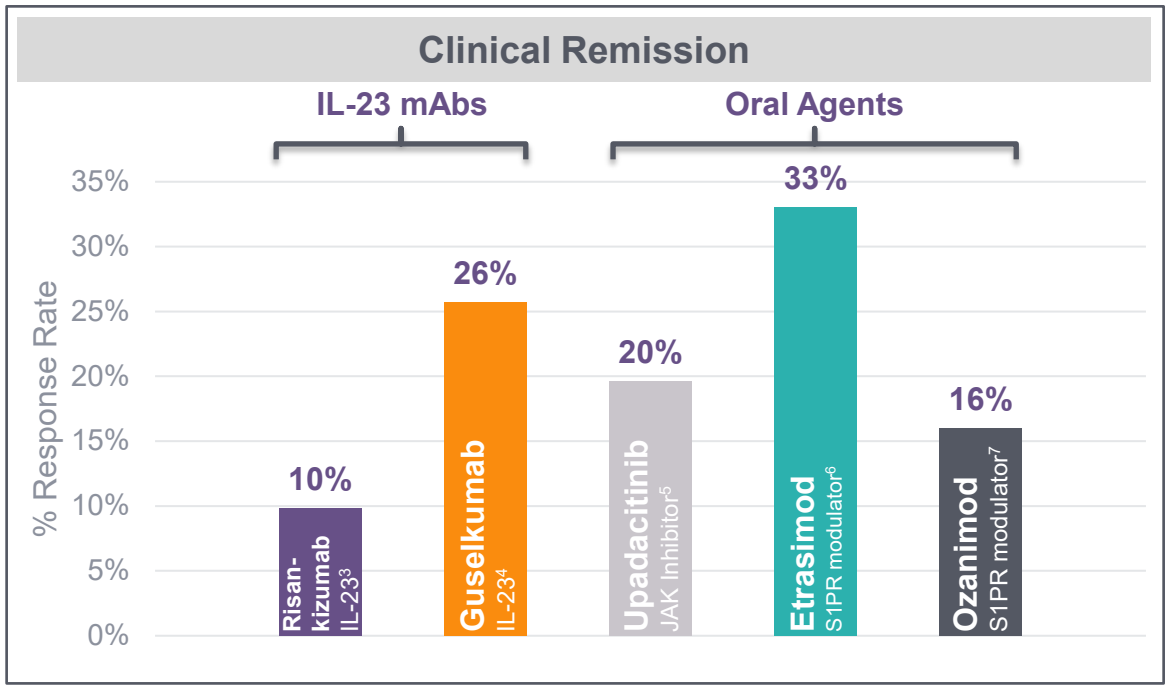


* Primary Completion Date on clinicaltrials.gov

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

Protagonist Therapeutics

Rusfertide: A Potential Practice-Changing, New Standard-of-Care in Polycythemia Vera (PV)

PV: A rare myeloproliferative neoplasm characterized by excessive production of red blood cells[1]

- Primary treatment goal is to maintain Hct <45%[2,3,4]

Polycythemia Vera. 1. 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.

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

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

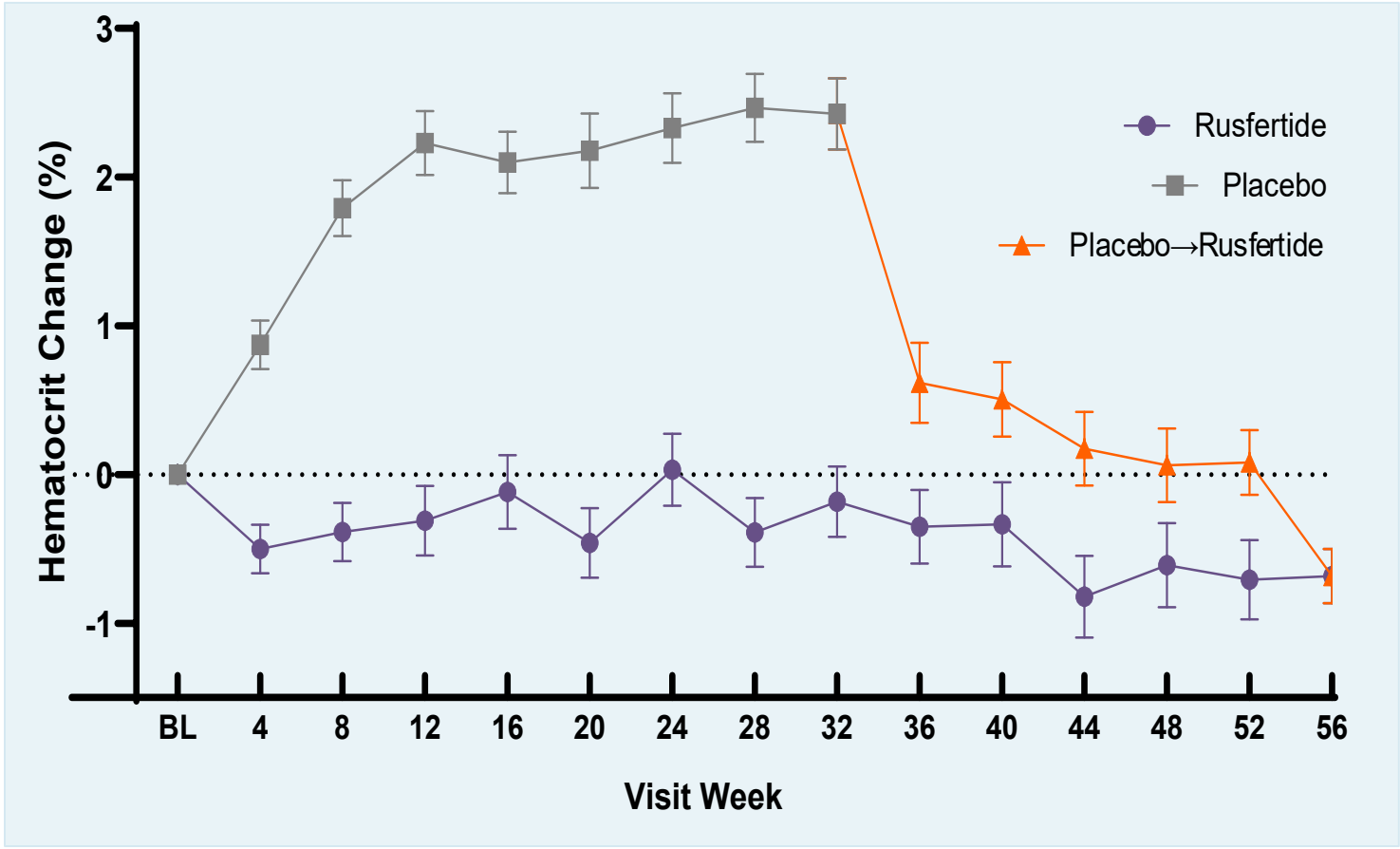
1. Marchioli R, et al. *N Engl J Med.* 2013;368:22-33.
2. Verstovsek S, et al. *Ann Hematol.* 2023;102(3):571-581.
3. Kaifie A, et al. *J Hematol Oncol.* 2016;9:18.
4. Griesshammer M, et al. *Ann Hematol.* 2019;98(5):1071-1082.
5. Polycythemia vera: the natural history of 1213 patients followed for 20 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.

Rusfertide Phase 3 VERIFY Study Results: PV[1,2]

Durable, Sustained Hct Control With Fewer PHLs vs. Placebo, Addressing Major Unmet Need in PV[1,2]

- **Primary endpoint:** Wks 20-32
  1. Clinical Response: rusfertide vs placebo ($p<0.0001$) ✓
- **Key 2° endpoints:** Wks 0-32
  1. Average number of PHLs ($p<0.0001$) ✓
  2. Proportion of patients with Hct <45% ($p<0.0001$) ✓
  3. Average PROMIS Fatigue SF-8a Score ✓
  4. Average MFSAF Total Symptom Score ✓

Rusfertide was generally well-tolerated through 52 Weeks of treatment. The most common treatment-emergent adverse events (AE) in rusfertide-treated patients were injection site reactions (47.4%), anemia (25.6%) and fatigue (19.6%), which were primarily grade 1 or 2. Serious AEs occurred in 8.1% of overall rusfertide-treated patients.



VERIFY featured in **Plenary Presentation** at ASCO'25

Hct, hematocrit; PHL, phlebotomy; PV, polycythemia vera.

1. Kuykendall AT, et al. *J Clin Oncol* 2025;43(LBA3); 2. Kuykendall AT, et al. *Blood* 2025;146(Suppl 1):81.

Rusfertide: An RBC-Centric Treatment Option for PV

Peak Revenue Potential of $1-2 Billion[3]

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

Treatment Paradigm

Patients are often on polytherapy and will cycle through various treatments[1]

~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[2]**
- **Rusfertide expected to be used at each step[3]**

Rusfertide provides consistent hematocrit control and can potentially reduce treatment burden to achieve **peak revenue potential of $1-2B[3]**

1. Komodo Health closed claims dataset (2016-2023); Note: ~2,000 patients are treated via a combination of other therapies.
2. Verstovsek S, et al. Real-world treatments and thrombotic events in polycythemia vera patients in the USA. Ann Hematol. 2023 Mar;102(3):571-581
3. Takeda FY2025 Q2 Earnings Release.

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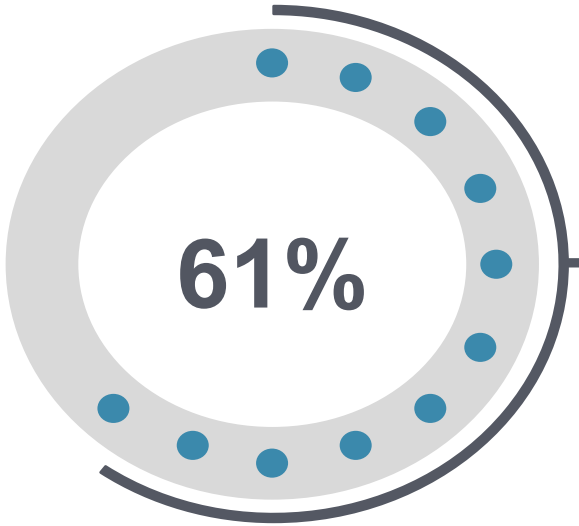
Most Patients With Polycythemia Vera Experience Suboptimal Hct Control

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



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 ≥1,000 mg HU per day

8% **Combination of PHL and HU**

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

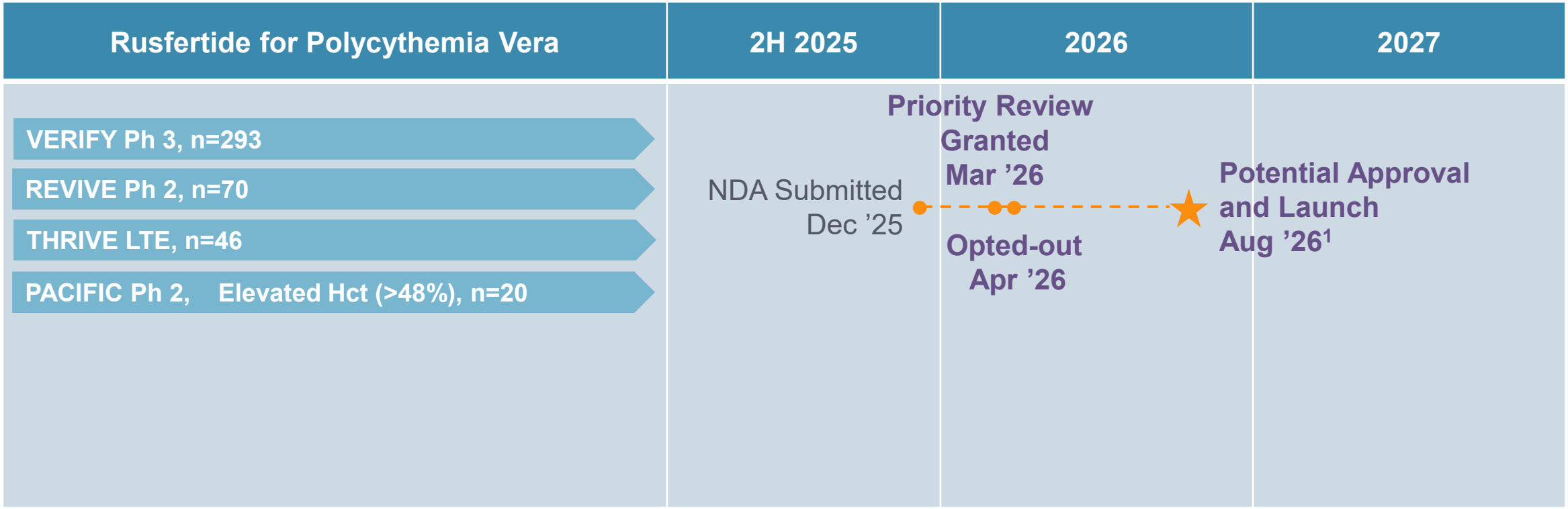
Komodo Health claims database (data from January 2016 to December 2022); includes patients who were ≥18 years old and had at least two clinical diagnoses of PV that were at least 6 months apart.

1. Kuykendall A, et al. *Expert Rev Hematol*. 2025;Epub ahead of print.

Protagonist Therapeutics

Rusfertide for PV: NDA Filing, Approval and Commercialization Launch Timelines

FDA Granted Rusfertide NDA Priority Review in March 2026



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

Potential FDA approval and commercial launch beginning in Aug 2026

1. Takeda Pharmaceutical Co., Ltd. Q1 2026 Earnings Call. 30 July 2026.

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

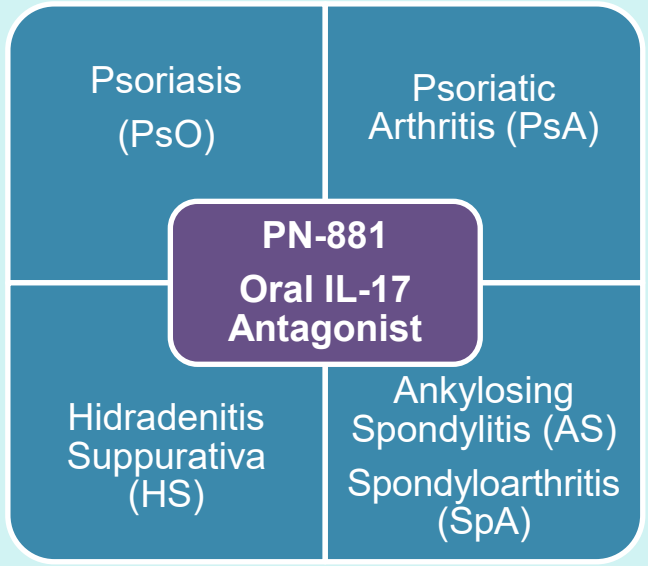
Targeting a $17B+ Market Opportunity with Differentiated ORAL IL-17 Inhibition

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

IL-17: Validated Market Opportunity[1]

- ***30% of PsO market*** by 2034
- ***$17B+ opportunity*** **currently** dominated by injectables

Strategic Indication Expansion



PN-881: Differentiated Target Product Profile

PN-881 Blocks All Three IL-17 Dimers

- ***Oral Peptide***
- ***Triple specificity***[2] matching Bimzelx profile
- Potential ***best-in-class profile***

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

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1. Psoriasis Disease Landscape and Forecast (Clarivate, Sept 2025); Evaluate Pharma.
2. 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

Criteria for Nomination of Oral PN-881 Development Candidate[1]

Oral PN-881 Achieved all Defined Criteria for 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

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

PN-881 Achieved Desired Pharmacology in Preclinical Models

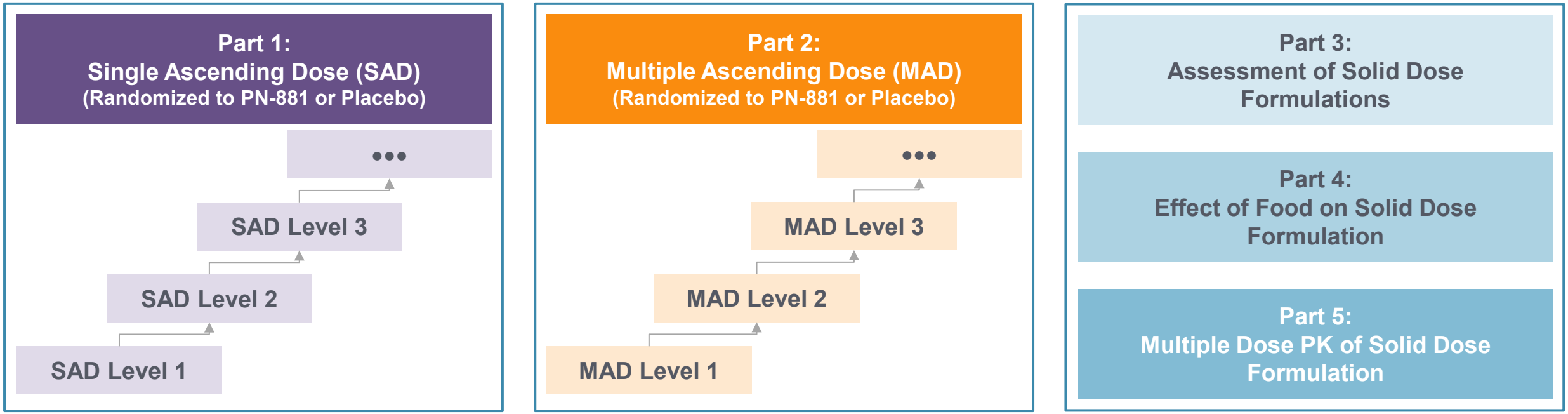
- High systemic exposures after oral administration to mice, rats, dogs, and cynomolgus monkeys
  - >100 ng/mL in cynomolgus monkeys with oral dose of 2.5 mg/kg

- 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: 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

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.

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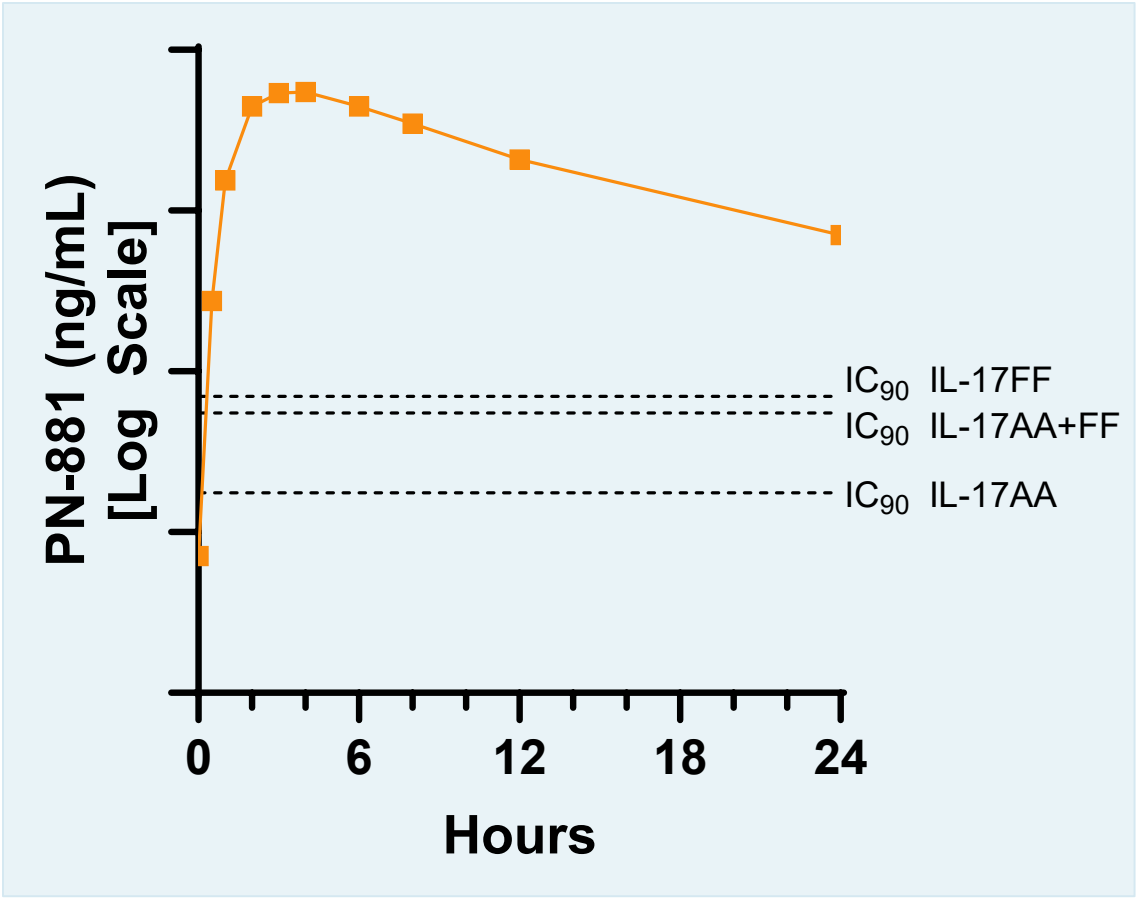
Data on File. Protagonist Therapeutics, Inc.

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

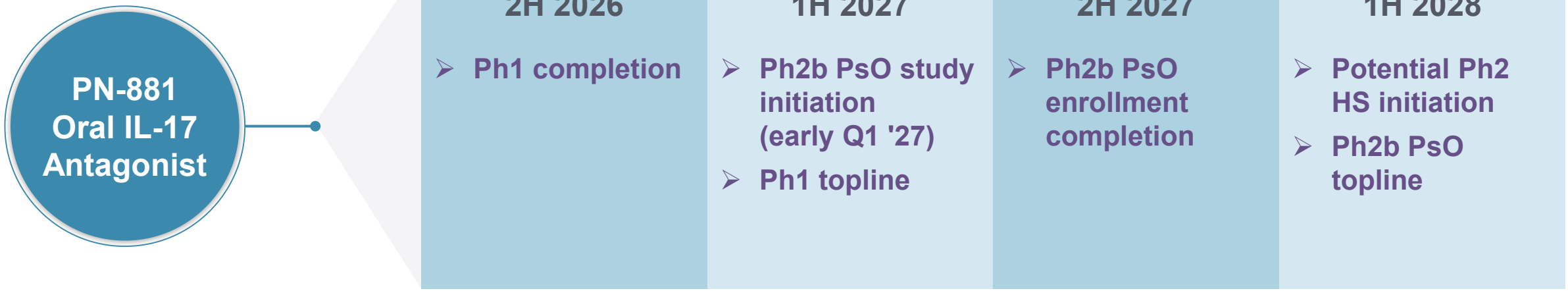


PN-881 Plasma Concentrations Several Fold Higher Than IC_{90} Values For Both Isoforms (AA & FF) and IL-17AA+FF

Protagonist Therapeutics

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

Clinical Development Plans in Psoriasis and Other Potential Indications



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

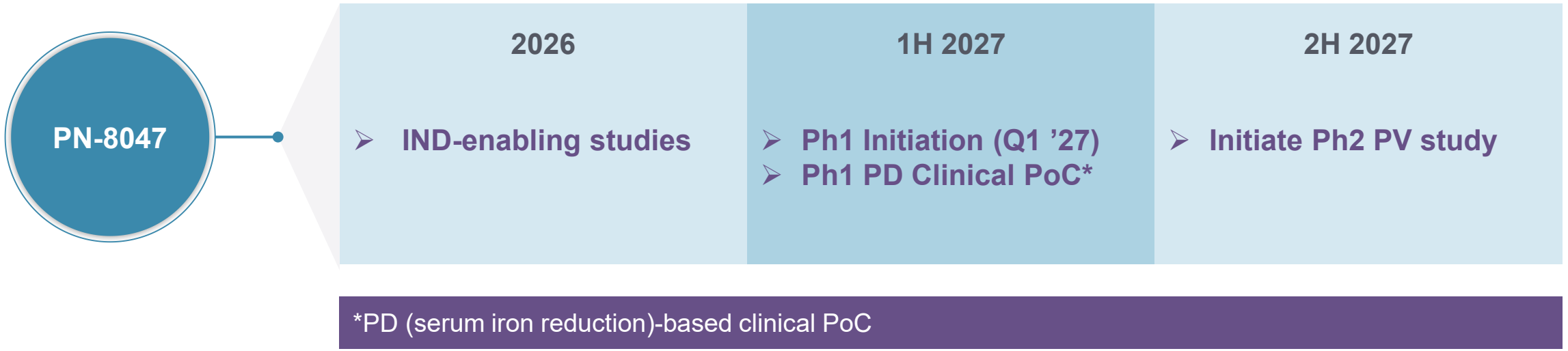
PN-8047: Novel Potent Oral Small Molecule With Excellent PK, PD, and Efficacy Properties

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

Protagonist Therapeutics

PN-8047: Oral Hepcidin Functional Mimetic Development Timelines



Protagonist Therapeutics

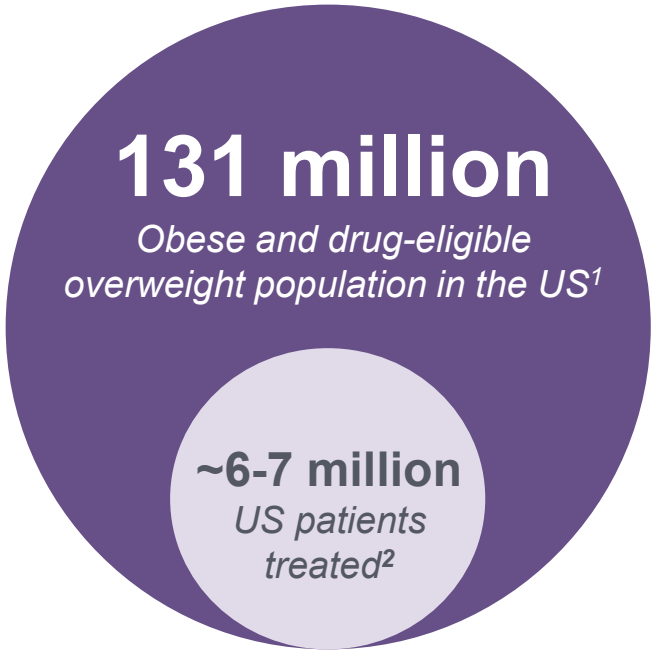
Metabolic Pipeline: Addressing the Need For Unimolecular Oral Anti-Obesity Therapies

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
  - 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.

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

Optionality for Oral or Subcutaneous Dosing

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)
- Maximize **optionality** of one drug substance with two formulations (oral or sc injectable)

ORAL Triple-Agonist Once-daily Dosing → **PN-477o**

Injectable Triple-Agonist Once-weekly Dosing → **PN-477sc**

Protagonist Therapeutics

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

PN-477 Oral Triple Agonist (GLP-1R, GIPR, GCGR) 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
Efficacy Model	✓ Mouse Diet Induced Obesity (DIO) model
in vivo Pharmacodynamics	✓ Glucose control with 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 More Potent than Retatrutide

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

- cAMP assay: PN-477 is more potent than retatrutide for GLP-1R and GIPR
  - GLP-1R : GIPR potency ratio for PN-477 is similar to tirzepatide

PN-477 is a novel, orally stable, and potent Triple-G agonist peptide, with a potency profile that combines the best of retatrutide for weight loss (GCGR activity), and of tirzepatide for tolerability (GLP-1R:GIPR potency ratio)

Protagonist Therapeutics

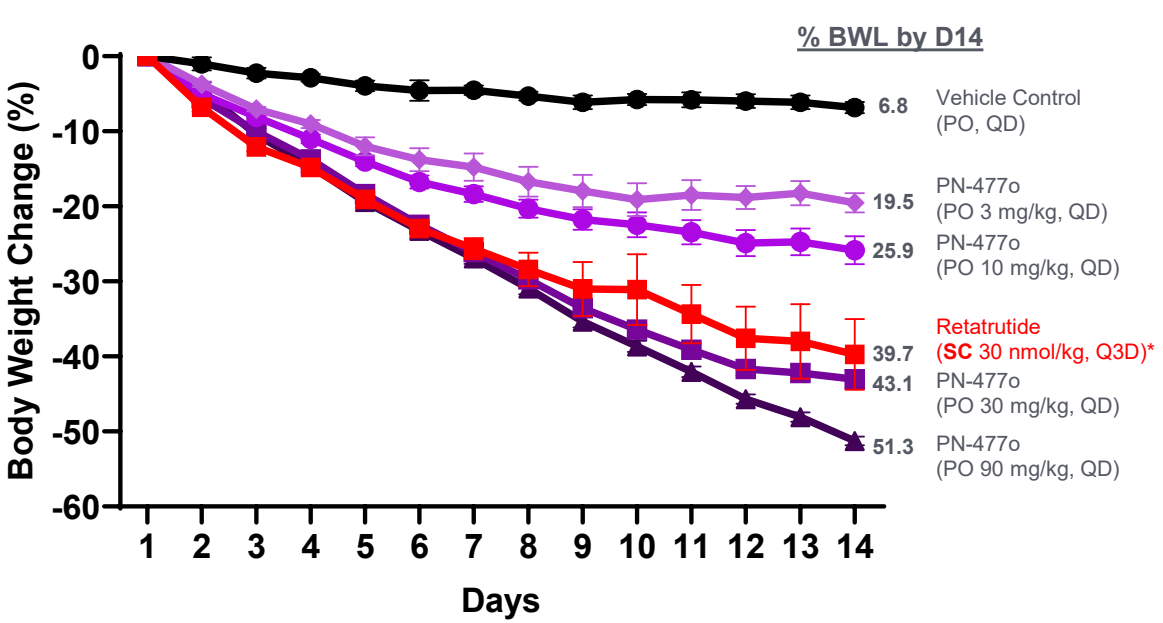
[1] Lau J, J Med Chem 2015; [2] Coskun T, Mol Metab 2018; [3] Coskun T, Cell Metab 2022

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

Oral and Subcutaneous PN-477 Promote Significant Body Weight Loss

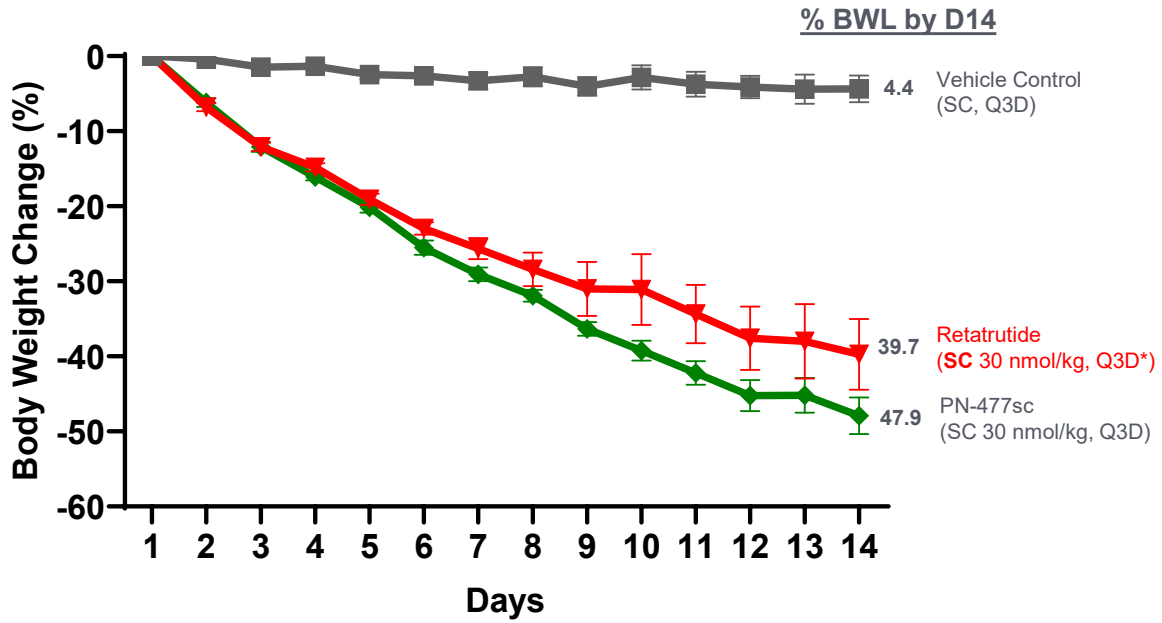
Pre-Clinical Efficacy Study Using DIO Mice

% 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.

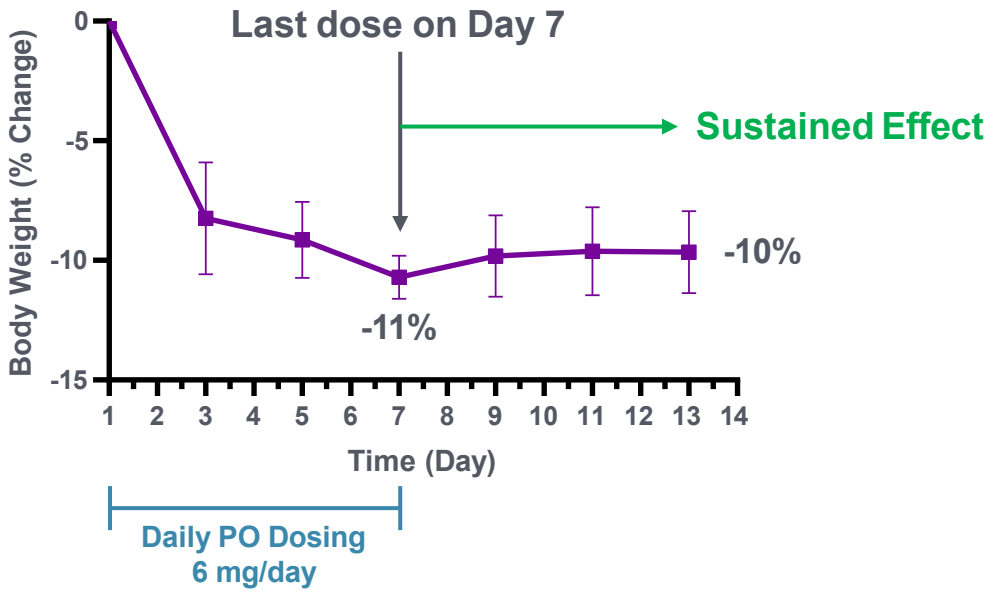
Data points depict mean ± SEM.

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

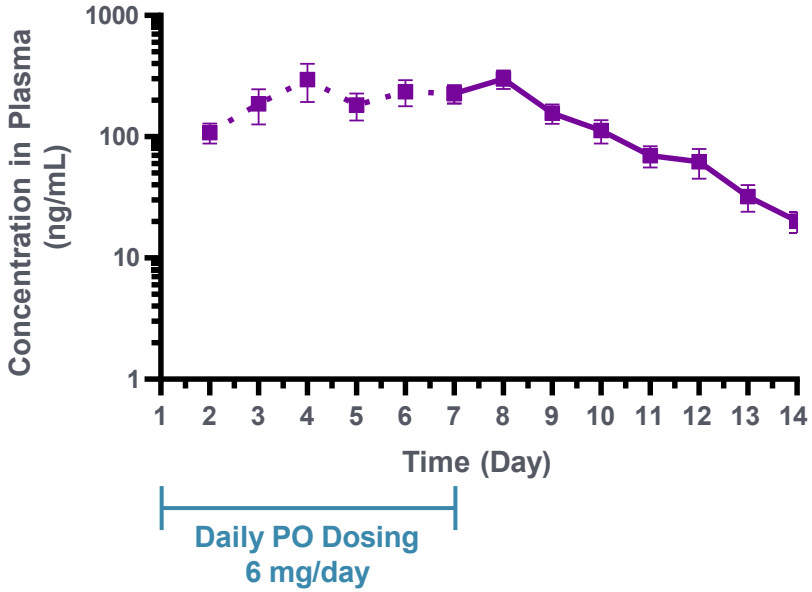
11% BW Loss by Day 7 in Normal Cynomolgus Monkeys after 7-Day Oral Dosing of PN-477

Weight Loss Sustained for 6 Days After Last Dose

% BW Change, PO



PK C_{trough} Day 1-7, PO



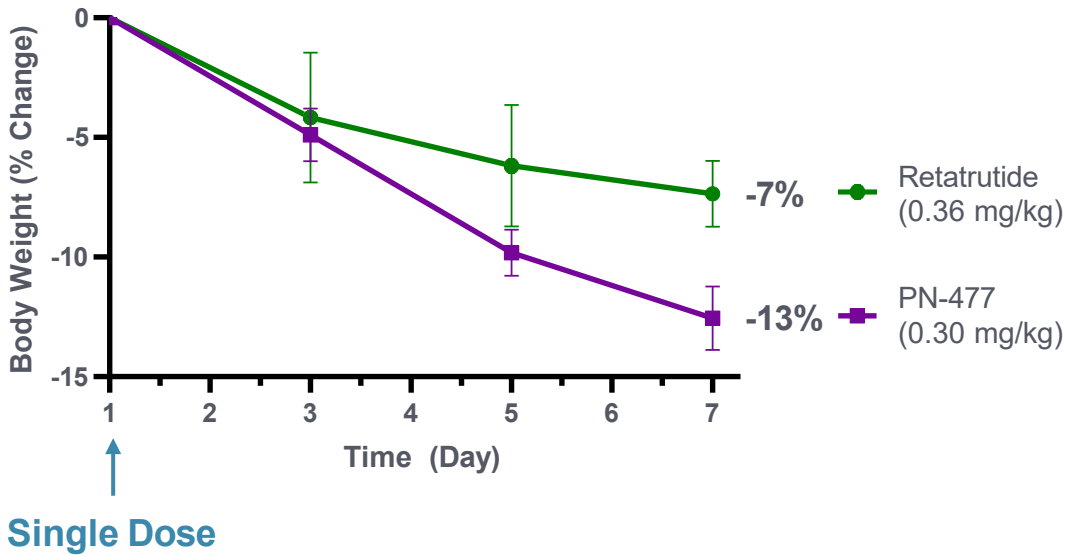
Oral PN-477 PK profile suggests **once daily human dosing and sustained weight loss**

Protagonist Therapeutics

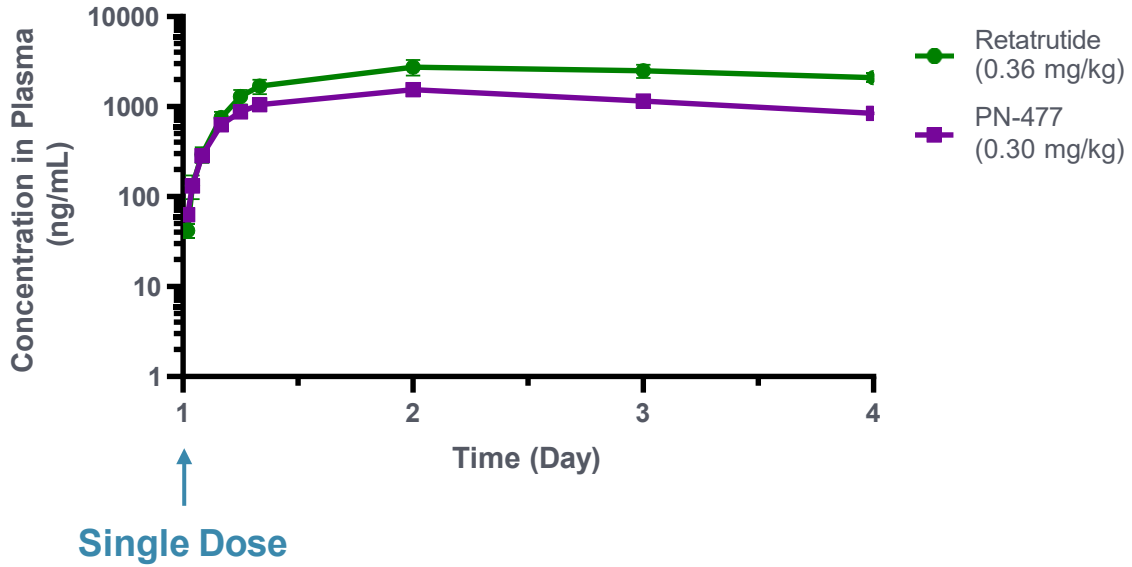
BW, Body Weight; PO, Per Os (oral); PK, Pharmacokinetics

13% BW Loss Normal Cynomolgus Monkeys by 7-Days Post-Single SC Dose of PN-477

% BW Change, SC



PK, SC

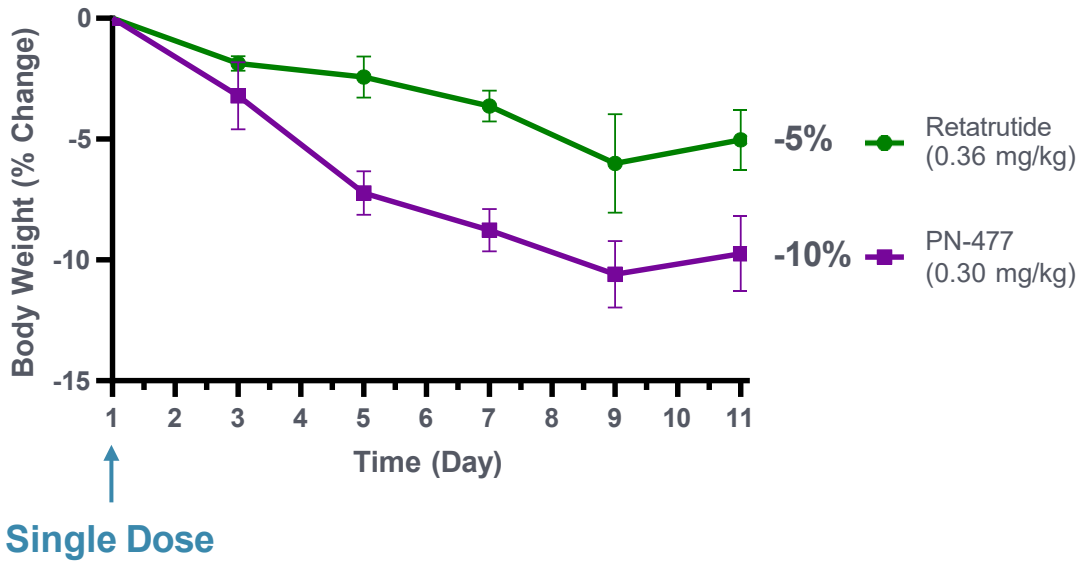


PK profile of subcutaneous PN-477 in cynomolgus monkeys suggests **once weekly human dosing**

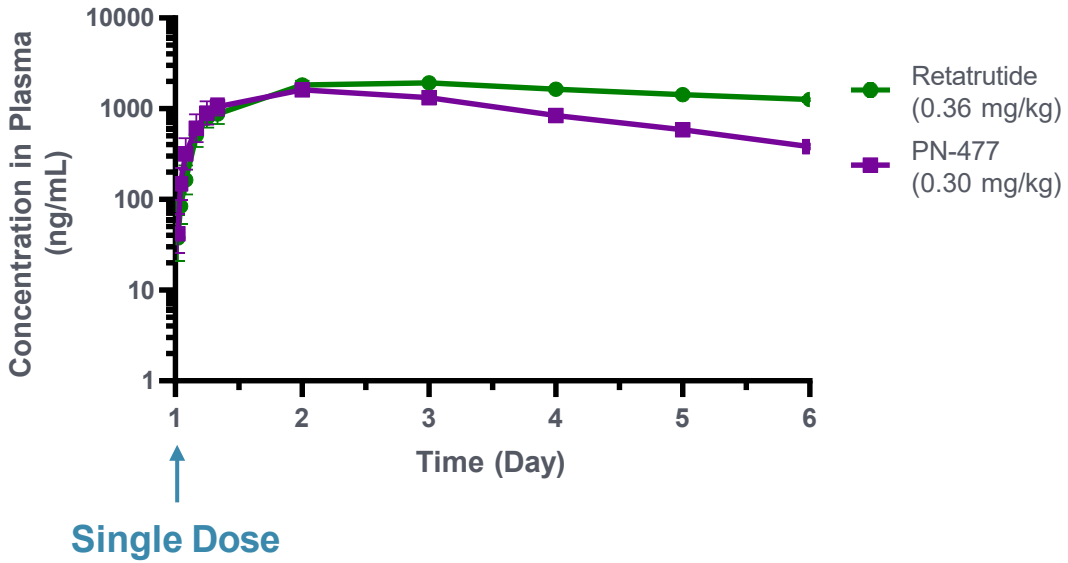
BW, Body Weight; PK, Pharmacokinetics; SC, subcutaneous

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

% BW Change, SC



PK, SC



Data from a single subcutaneous dose of PN-477 in normal weight dogs supports once-weekly dosing in humans

Protagonist Therapeutics

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

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

- Novel, orally stable, and potent triple agonist (GLP-1R, GIPR, and 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
- Phase 1 study initiated with PN-477sc

PN-477: Near-Term Clinical Development Plan

PN-477sc* Anti-Obesity

2026	1H 2027	2H 2027
❖ PN-477sc Ph1 SAD initiated (Q3 ’26)	❖ PN-477sc Ph1b MAD (13 weeks) initiation	❖ PN-477sc Ph1b MAD PoC

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-477sc: weekly sc dosing; PN-477o: once-daily oral dosing

Protagonist Therapeutics

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

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	✓ Mouse Diet Induced Obesity (DIO) model
In vivo Pharmacodynamics	✓ Glucose control 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

GI: Gastrointestinal; PK: Pharmacokinetic

IND-enabling studies in progress

Protagonist Therapeutics

Two Anti-Obesity Assets Create Strategic Flexibility

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

PN-477

TRIPLE AGONIST

GLP-1 / GIP / GCG agonist peptide

DESIGN GOAL	**Maximize weight loss magnitude and quality (preferential fat mass loss)**
BENCHMARK	**Retatrutide-class profile**
FORMATS	**Once-daily oral, once-weekly SC**
PRECLINICAL	**Significant body weight loss in DIO mice, dogs, and cynomolgus monkeys**

PN-458

DUAL AGONIST

GLP-1 / GIP agonist peptide

DESIGN GOAL	**Balance weight loss with GI tolerability**
BENCHMARK	**Tirzepatide-class profile**
FORMATS	**Once-daily oral**
PRECLINICAL	**Significant body weight loss in DIO mice, dogs, and cynomolgus monkeys**

Protagonist Therapeutics

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

Protagonist Therapeutics

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 ❖ EMA CHMP Positive Opinion: July 2026	❖ Commercial
Rusfertide Partner: Takeda	❖ NDA accepted; priority review granted ❖ Opted-out	★ **Potential US approval/launch for PV**	❖ Commercial
PN-881*	Oral IL-17 antagonist ❖ Ph1 ongoing	❖ **Ph1 completion**	❖ **Comprehensive Ph2b PsO Initiation (early Q1 '27)** ❖ **Ph1 data** ❖ Potential Ph2 Initiation (eg, HS)
PN-477sc* **PN-477o***	Anti-obesity DCs ❖ IND-enabling studies	❖ **PN-477sc Ph1 SAD initiation**	❖ **PN-477sc Ph1b MAD Initiation and PoC** ❖ **PN-477o Ph1 SAD (1H '27)** ❖ **Ph1b MAD initiation (2H '27)**
PN-8047*	Oral Hepcidin DC ❖ IND-enabling studies	❖ IND-enabling studies	❖ 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		

*Wholly-owned by Protagonist Therapeutics, Inc. DC, Development candidate, ready for IND-enabling studies; IND, investigational new drug; MAD, multiple ascending dose; NDA, new drug application; PD, pharmacodynamic; PoC, proof of concept; PsO, psoriasis; SAD, single ascending dose.

Protagonist Therapeutics

Thank you