Protagonist Therapeutics

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"), enrollment in our VERIFY Phase 3 clinical trial, potential future collaboration arrangements, our IL-17 and other discovery and pre-clinical programs, our potential receipt of milestone payments and royalties under our Collaboration Agreement with Janssen Biotech, Inc. ("Janssen") related to JNJ-2113, the timing of JNJ-2113 clinical results, Janssen's development plan for JNJ-2113, and the potential market opportunity for rusfertide and JNJ-2113, 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.

The forward-looking statements made in this presentation involve known and unknown risks, uncertainties and other important factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements. These forward-looking statements are subject to risks and uncertainties, including those discussed in Protagonist's 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 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. Except as required by applicable law, we do not plan to publicly update or revise any forward-looking statements contained herein, whether as a result of any new information, future events, changed circumstances or otherwise.

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Core Competency Remains our Focus

Expertise in Peptide-based Medicines

Potency

1 **Computational**
Vectrix, Clusters

2 **Phage Libraries**
Hits

3 **Peptide Chemistry**
SAR, Leads

Stability

4 **Oral Stability**
Peptidomimetics
GI Assays

2 **GI-Restricted**
Targeted GI
absorption & delivery

3 **Systemic Availability**
Formulation
SAR, Transport

Rusfertide in PV Ph3

JNJ-2113 Psoriasis Ph3

Oral IL-17 Discovery

NEW

Protagonist Therapeutics

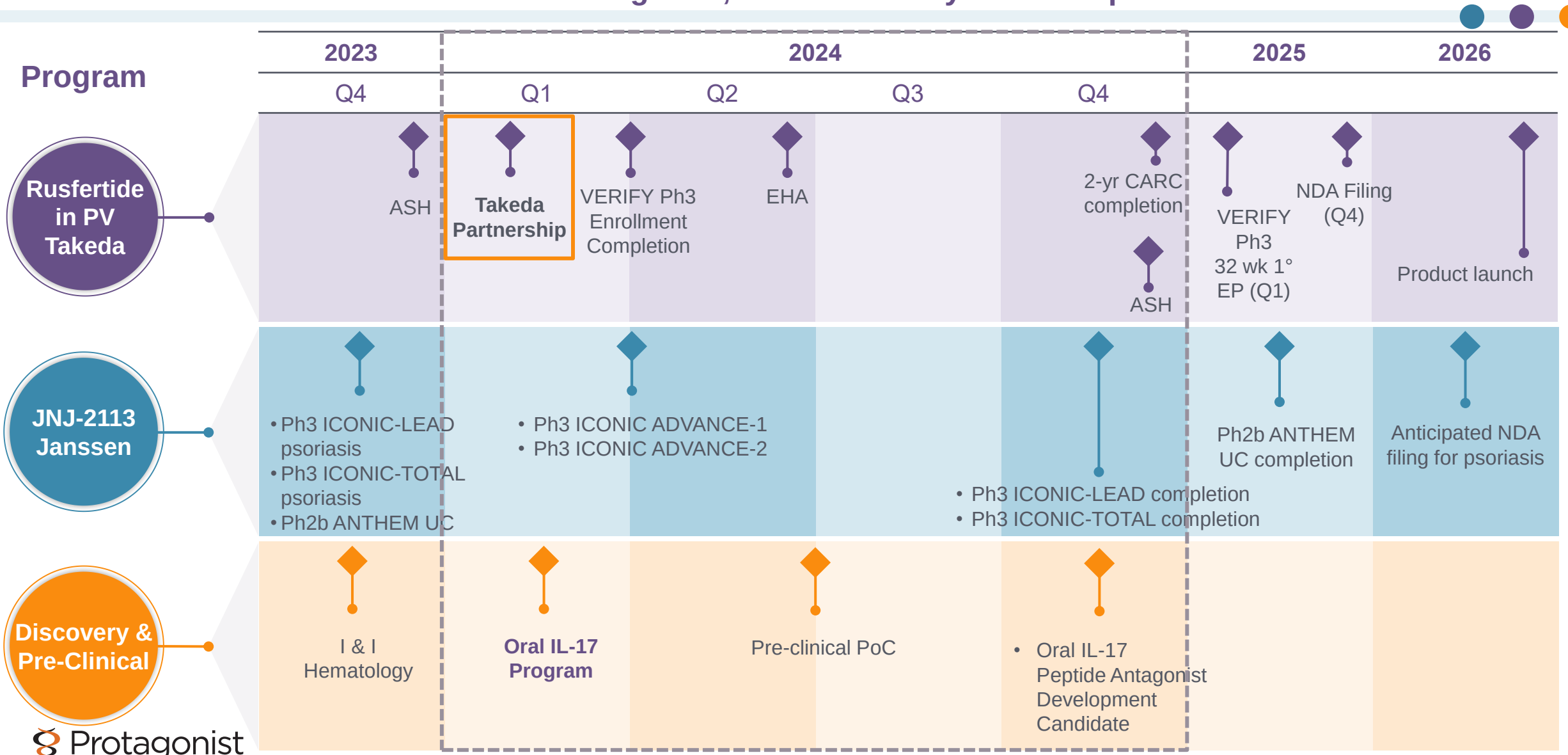
Product Pipeline: Multiple Assets with Multi-Billion Dollar Market Potential

		Disc./Pre-Clinical	Phase 1	Phase 2	Phase 3	Key Milestones
HEMATOLOGY	Protagonist Therapeutics / Takeda RUSFERTIDE	**Polycythemia Vera (PV)**				
		VERIFY Ph3, n~250				• Enrollment completion by end of 1Q 24
		REVIVE Ph2, n=70, 40 wk study + 3 yr OLE				• Completed; OLE ongoing
		THRIVE LTE				• For REVIVE patients on years 3-5
		PACIFIC Ph2 Elevated Hct (>48%), n=20				• Completed
I & I	janssen JNJ-2113 Oral IL-23R Peptide Antagonist	**Psoriasis**				
		FRONTIER 1 & 2 Ph2b, n~255				• Completed
		ICONIC-LEAD Ph3, n~600				• Primary: PASI 90 & IGA 0/1; completion ~ Nov '24[1]
		ICONIC-TOTAL Ph3 in special areas of psoriasis, n~300				• Primary: IGA 0/1; completion ~ Nov '24[2]
		ICONIC- ADVANCE 1 Ph 3, n~750				• JNJ-2113 vs. deucravacitinib; completion ~ Mar '25[3]
		ICONIC- ADVANCE 2 Ph 3, n~675				• JNJ-2113 vs. deucravacitinib; completion ~ Apr '25[4]
		Ulcerative Colitis (UC)				
		ANTHEM Ph2b, n~240				• Primary Completion ~ May '25[5]
DISCOVERY	Protagonist Therapeutics Discovery	Oral IL-17				• Oral IL-17 peptide antagonist program[6]
		HEME				• Hits/Leads in heme program

1 See clinicaltrials.gov NCT06095115
2 See clinicaltrials.gov NCT06095102
3 See clinicaltrials.gov NCT06143878
4. See clinicaltrials.gov NCT06220604
5. See clinicaltrials.gov NCT06049017
6. Development Candidate by end of 2024

Major Catalysts Ahead

A Transformative Path Forward for Protagonist, from Discovery to Development to Commercialization



Protagonist Therapeutics

Protagonist Therapeutics

Rusfertide
Hepcidin Hormone Mimetic

Addressing Unmet Needs in
Polycythemia Vera

Rusfertide

Takeda and Protagonist Collaboration, Jan 31, 2024

- Co-development and Co-commercialization partnership with 50:50 profit/loss share in US
  - Takeda has exclusive Ex-US global rights
  - Protagonist responsible for R&D through Phase 3 completion and NDA filing
  - Takeda responsible for pre-commercial activities
  - Up-front payment of $300M

- Protagonist has the right to remain (**OPT-IN**) in the US 50:50 profit share, or to **OPT-OUT** post-NDA filing

Scenario	Total	Upfront	Payable Opt-Out	Potential Milestones	Royalty Rates	Comment
OPT-IN	$630M	$300M	-	$330M	10-17%	• 50:50 US profit/loss share • Royalties on Ex-US net sales
OPT-OUT	$1,675M	$300M	$400M	$975M	14-29%	• No US profit/loss share • Royalties on Worldwide net sales

Polycythemia Vera

Disease Background

Myeloproliferative neoplasm characterized by excessive production of red blood cells (RBCs)[1]

- Elevated hematocrit (Hct) is a hallmark of the disease, indicating overproduction of RBCs[2]

Serious, chronic disease associated with increased thrombotic and cardiovascular risks[1-3]

Rare disease with ~100,000 diagnosed and treated patients in US[1]

- Diagnosed commonly in individuals 50-70 years of age
- Median survival ~20 years

Treatment goal is to control

HCT<45%

to minimize TEs, CV events and death[3]

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

Protagonist Therapeutics

The Unmet Need in PV is Three-Fold

Inconsistent Hct Control, Iron Deficiency, and Symptom Burden

Inconsistent Hct Control

- Maintaining Hct <45% is critical, as uncontrolled Hct is associated with ~4 times higher rate of death from cardiovascular causes or thrombotic events[2]
- Real-world data shows that 78% of patients have uncontrolled Hct with tests ≥45%[1]

Iron Deficiency

- Most patients with PV are iron deficient due to depleted bone marrow iron levels[3]
- Some treatments exacerbate disease-related symptoms by inducing iron deficiency[3,4]
- There is no pharmaceutical option with RBC-specific mechanism

Symptom Burden

- Patients have burdensome symptoms, including fatigue and concentration problems[5]
- 84% of patients report fatigue, and 23% report spending full days in bed because of symptoms[6]
- PV impacts reported activities of daily living and productivity[5]

1. Verstovsek S, et al. Ann Hematol. 2023 Mar;102(3):571-581 2. Marchioli R, et al. N Engl J Med 2013; 368:22-33 3. Verstovsek S, et al. Leuk Res. 2017;56:52-59. doi:10.1016/j.leukres.2017.01.032. 4. McMullin MF, et. al. Br J Haematol. 2019 Jan; 184(2): 176-191. 5. Mesa R, et al. BMC Cancer. 2016;16,167. 6. MPN Landmark Survey, PV Report (2017).

Hydroxyurea is the Gatekeeper to Other Agents in PV

HU, used alone or in combination with phlebotomy, is the most common 2nd and 3rd line PV therapy[1]

Many patients require high doses of HU, but still experience inadequate Hct control

- 60% of patients receiving HU require ≥1,000mg daily[1]
- 35% of patients receiving HU experience Hct ≥45%[2]
- Some patients may be intrinsically resistant to HU, making even high doses ≥2,000mg ineffective[2]

HU is associated with potentially serious side effects and adverse events[3]

- Myelosuppression may lead to anemia, leukopenia, and thrombocytopenia, especially at high doses
- Long-term use of HU can cause secondary leukemias and skin cancers

Sub-optimal efficacy and safety of HU illustrates an unmet need for PV patients with elevated Hct that cannot be managed without frequent phlebotomies

Protagonist Therapeutics

1. Komodo claims data 2016-2022. 2. Parasuraman S, et al. Exp Hematol Oncol 2015; 5(3). doi:10.1186/s40164-016-0031-8. 3. Jinna S and Khandar PB. NIH 2022. https://www.ncbi.nlm.nih.gov/books/NBK537209/.

Marketed Agents for PV are Cytoreductive Therapies

No Approved Medications That Specifically Target Red Blood Cells and Hematocrit

Interferon

Pegasys®, Besremi®

Interferons have long been used off-label in PV treatment; Besremi is the first interferon product approved for PV[1]

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

Failed to show noninferiority to HU at 12 months in the PROUD-PV study[3]

Black box warning for serious neuropsychiatric, autoimmune, ischemic, and infectious disorders[2]

Ruxolitinib

Jakafi®

Only approved for hydroxyurea-resistant or intolerant patients[4]

Improves splenomegaly, a potential marker of disease progression[5]

Potential serious side effects include thrombocytopenia, neutropenia, and anemia[4]

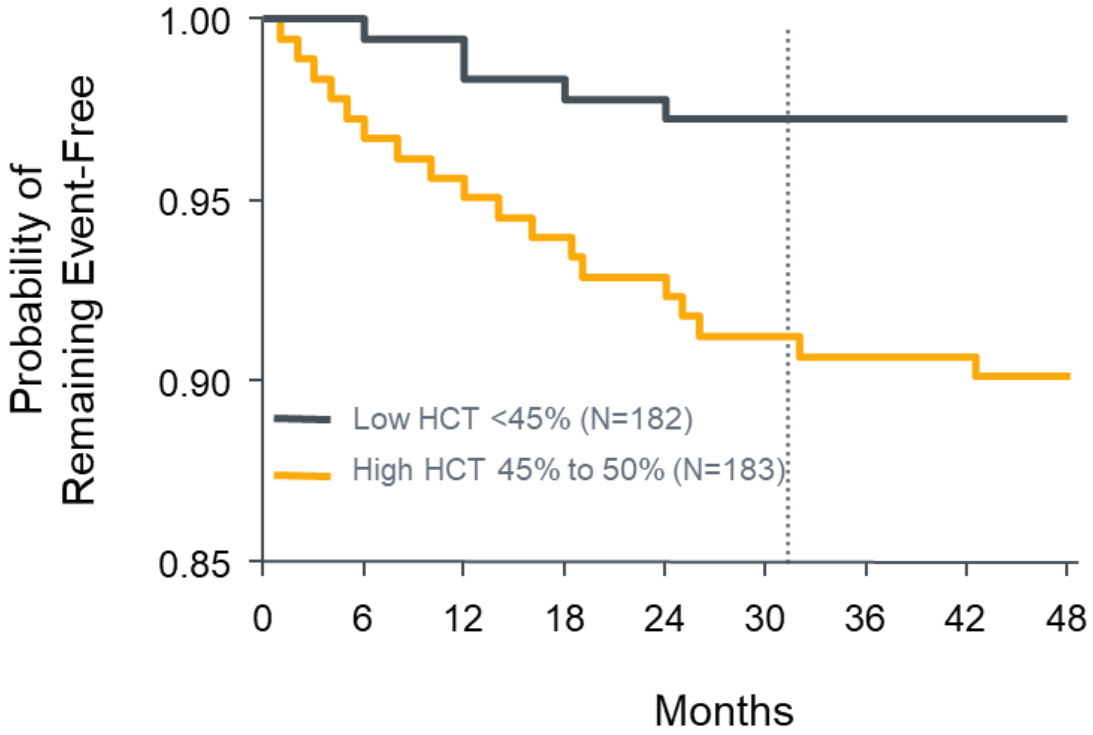
23% of patients were found to have discontinued ruxolitinib within a mean of **2 years** post treatment initiation[6]

1. Gilreath JA, et. al. Blood. 2018;132 (Supplement 1). 2. Besremi FDA label. 3. Gisslinger H, et. al. Lancet Haematol. 2020;7(3):e196-e208. 4. Jakafi FDA label. 5. Coltoff R, et. al. Clin Lymphoma Myeloma Leuk. 2020;20(10): 697-703. 6. Tremblay, D. Leuk Res. 2021;109.

Increased Hematocrit is Associated with Increased Morbidity and Mortality

Current Treatment Options are Inadequate

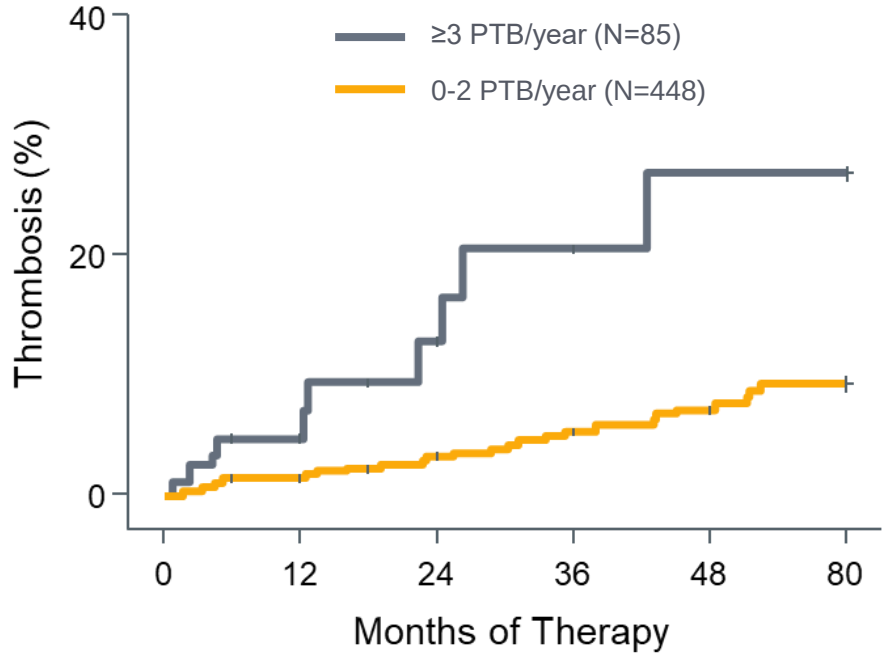
Elevated Hematocrit Contributes to ~4x Increased Risk of CV Death and Major Thrombosis



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

Phlebotomy, Even with Concomitant Cytoreductive Therapy, Is Inadequate in Reducing Thrombotic Risk

All HU-treated (*P<0.0001*)



Alberto Alvarez-Larran et al. Haematologica 2017; 102:103-109

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Thromboembolic Events are Associated with PV

- In observational studies, **patients with PV had higher rates of TEs** compared to matched controls (14.3 vs 4.9/1000 patient years)[1-3]
- In a retrospective analysis of US electronic health records contained in the Optum® MarketClarity database, TEs were evaluated in 20,000+ PV patients (date range: 2007-2019)[4]
  - Approximately **25% of PV patients experienced post-index TEs**
  - TE incidence was highest among event-based high-risk patients (50.2%), followed by age-based high-risk (25.0%) and low-risk patients (13.3%)

Parameter	Total cohort	Event-based high-risk	Age-based high-risk	Low-risk
Total	N=20,089	*n*=3256	*n*=9924	*n*=6909
Any TE, *n* (%)	5035 (25.1)	1634 (50.2)	2480 (25.0)	921 (13.3)

  - In PV patients with 5 years of follow-up data, high-risk patients had a greater risk of death than event-based low risk patients (37% vs 8.5%, respectively)
- **These data suggest that thrombotic risk reduction should be an area of focus across all PV risk groups**

Protagonist Therapeutics

PV, polycythemia vera; TE, thromboembolic event.

1. Goyal RK, et al. *Blood*. 2014;124:4840. 2. Griesshammer M, et al. *Ann Hematol*. 2019;98:1071-82. 3. Pemmaraju N, et al. *Leuk Res*. 2022;115:106809. 4. Kuykendall A, et al. *Blood* 2023; 142 (Supplement 1): 137.

Burden of Treatment Impacts Treatment Strategy

Guidelines Use Risk to Govern Treatment Strategy, but Treatment Burden Has Real-World Significance

Risk Stratification

- NCCN guidelines characterize PV patients as low- or high-risk, defined as:
  - Low-risk: age <60 years without history of TE
  - High-risk: age ≥60 years and/or history of TE
- Physicians often do not adhere to guidelines for low- and high-risk patients because this stratification is not comprehensive
- Other critical aspects of care, such as perceived **treatment burden**, influence one's treatment strategy

Treatment Burden

- **Treatment burden** is the impact of patient's therapy regimen on overall wellbeing
- Factors influencing treatment burden include:
  - Physical impacts (side effects, pain, inconvenience of therapy)
  - Psychological impacts (emotional burden, fear of complications)
  - Financial impacts
- According to HCP research, frequent PHL (≥3 in 6 months) and adverse events had the most significant impact on treatment burden

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Baseline AAU Study of Rusfertide, N=45 hematologist, oncologists, or hem/oncs interviewed

Identifying PV Patients with Moderate Treatment Burden

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

Key indicators of suboptimal control for a PV patient

Phlebotomy Frequency

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

Frequent phlebotomies may exacerbate iron deficiency and related symptoms[1]

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 malignancies[2]

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

Protagonist Therapeutics

1. McMullin MF, et. al. Br J Haematol. 2019; 184(2): 176-191. 2. Jinna S and Khandar PB. NIH 2022. https://www.ncbi.nlm.nih.gov/books/NBK537209/.
3. Stegelmann F, et al. *Leuk* 2021; 35(2):628-631. doi: 10.1038/s41375-020-0945-3.

Rusfertide for Polycythemia Vera

Successful Phase 2 Completion and Phase 3 Enrollment Nearing Completion

- Phase 2 **REVIVE** Study (n=70):
  - Randomized withdrawal data presented at EHA 2023[1] as a late breaker oral
    - 69% responder rate (vs. 19% placebo; p=0.0003)
  - Long-term extension data presented at ASH 2023[2]
    - Durable hematocrit control through 2.5 years
- Phase 2 **THRIVE** Study (n≈50):
  - Long-term extension study (for REVIVE patients on study years 3-5)
- Phase 2 **PACIFIC** Study (n=20)[3]:
  - High hematocrit (Hct >48%); 52-week open-label study completed in Q2 2023
- Phase 3 **VERIFY** Study (n≈250)[4]:
  - Enrollment completion expected in 1Q 2024
  - Primary endpoint essentially same as Phase 2; statistical powering geared for proving secondary endpoints
  - Secondary endpoints include multiple symptom improvement metrics

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

Protagonist Therapeutics

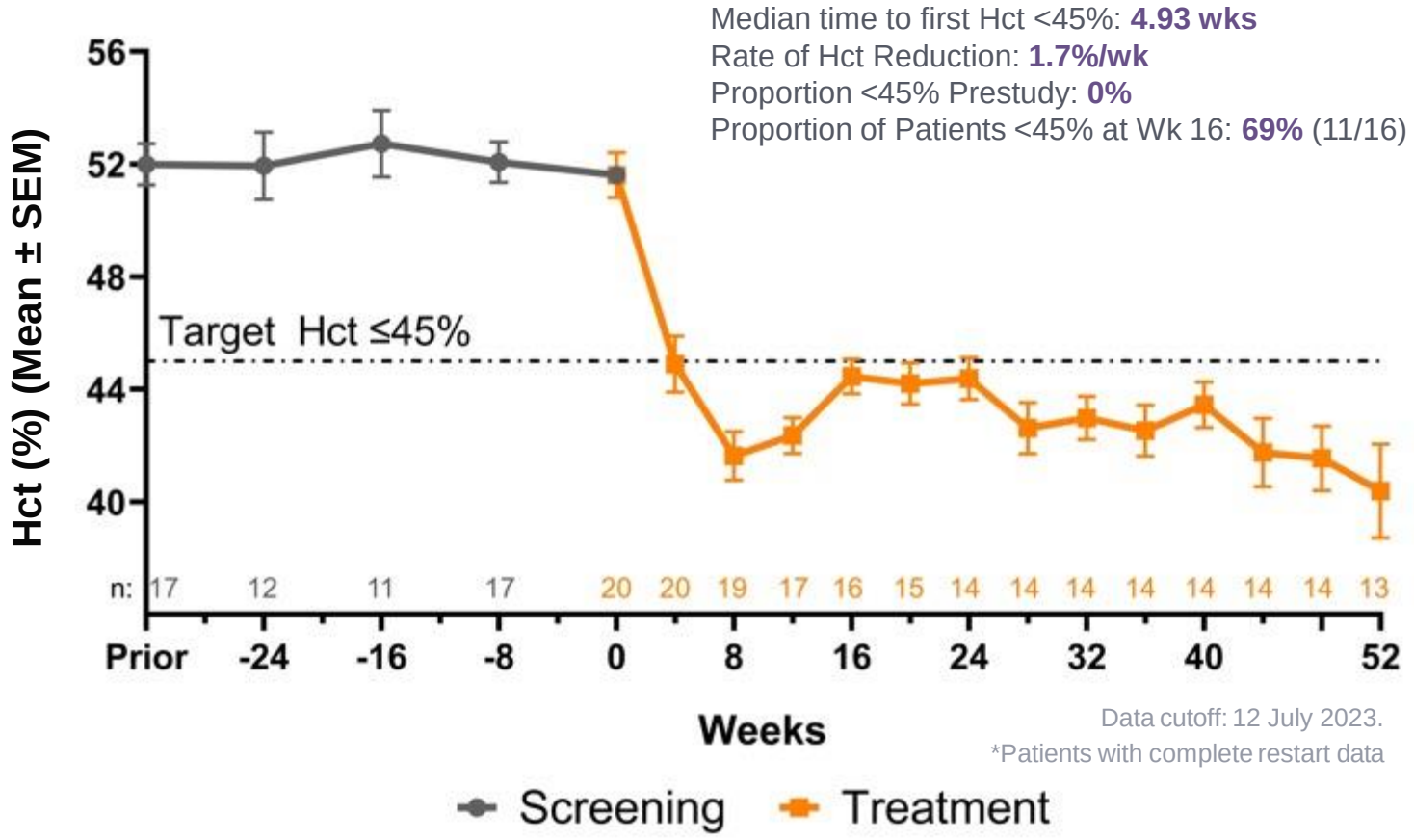
1. Kremyanskaya et al. EHA2023; Abstract LB2710; 2. Ritchie EK, et al. *Blood*. 2023;142 (Supplement 1): 745.; 3. Ginzburg Y, et al. *Blood*. 2023;142 (Supplement 1): 3208. 4. Verstovsek S, et al. *Blood* 2022; 140 (Supplement 1): 3929–3931.

Clinical Study of Rusfertide in PV Patients with High Hematocrit (>48%)[1,2]

Rapid Hematocrit Control <45% Was Achieved

Ph2 PACIFIC Study

- **Open-label, 1 year study in PV patients who are newly diagnosed or for whom current treatment is not sufficient to control hematocrit (Hct)**
- **Patients met WHO criteria for PV diagnosis**
  - Baseline Hct>48%
  - History of ≥3 Hct values >48% in prior 28 wks or ≥5 Hct values in prior year
  - Phlebotomy alone or with concurrent cytoreductive therapy
  - Initiated rusfertide treatment without prestudy phlebotomy
- **Clinical endpoints**
  - Proportion of subjects with Hct <45% at week 16
  - Time to first Hct <45%
  - Safety

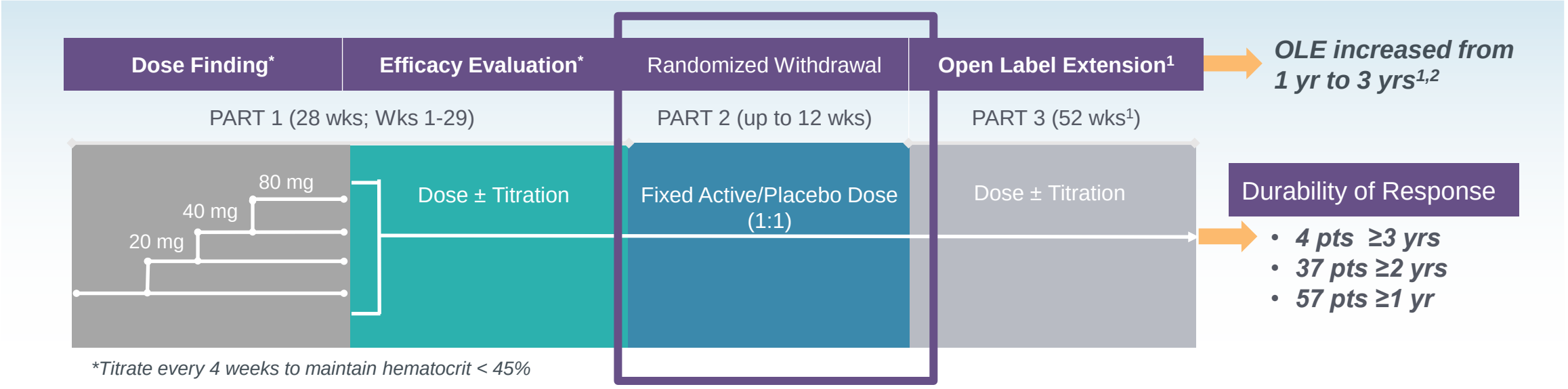


1. Adapted from Ginzburg Y, et al. Rusfertide Improves Markers of Iron Deficiency in Patients with Polycythemia Vera. *Blood*. 2023;142 (Supplement 1): 3208. 2. Data on File. Protagonist Therapeutics, Inc. 2023.

Phase 2 **REVIVE** Study of Rusfertide in PV Patients (n=70)

Randomized Withdrawal Design

Ph2 REVIVE Study



STUDY HIGHLIGHTS:

- Phlebotomy dependent PV patients diagnosed as per 2016 WHO criteria
- ≥3 phlebotomies in 6 months with or without concurrent cytoreductive therapy
- Rusfertide (PTG-300) administered s.c. weekly, added to prior standard therapy
- Key endpoints: Safety, Hct<45%, freedom from phlebotomy, symptom scores

Protagonist Therapeutics

1. Ritchie EK, et al. Durability of Hematocrit Control in Polycythemia Vera with the First-in-Class Hepcidin Mimetic Rusfertide: Two-Year Follow up Results from the Revive Study. *Blood*. 2023;142 (Supplement 1): 745. 2. Data on File. Protagonist Therapeutics, Inc. 2023.

Data cutoff: 17 October 2023

Baseline Characteristics

Characteristics (n = 70)

AGE	
Range	27-77 years (Median, 58)
GENDER	
Females	21 (30.0%)
Males	49 (70.0%)
RISK	
Low	30 (42.9%)
High	40 (57.1%) [Age based – 37.1%, Thrombotic events – 20.0%]
DURATION SINCE PV DIAGNOSIS	
≤1 yr	14 (20.0%)
1 - ≤3 yrs	23 (32.9%)
3 - ≤5 yrs	11 (15.7%)
>5 yrs	22 (31.4%)

CONCURRENT THERAPIES	
PHL only	37 (52.9%)
PHL + HU	18 (25.7%)
PHL + IFN	8 (11.4%)
PHL + JAK inhibitor	5 (7.1%)
PHL + Multiple Agents	2 (2.9%)
NUMBER OF PHL IN 28 WEEKS PRIOR	
2	1 (1.4%)
3	13 (18.6%)
4	26 (37.1%)
≥5	30 (42.9%)
Median	4 (2.9)
WEEKS BETWEEN PHLEBOTOMIES IN 28 WEEKS PRIOR	
Median	5.5

Data cutoff: 17 October 2023

Protagonist Therapeutics

Enrollment complete. Data on File. Protagonist Therapeutics, Inc.

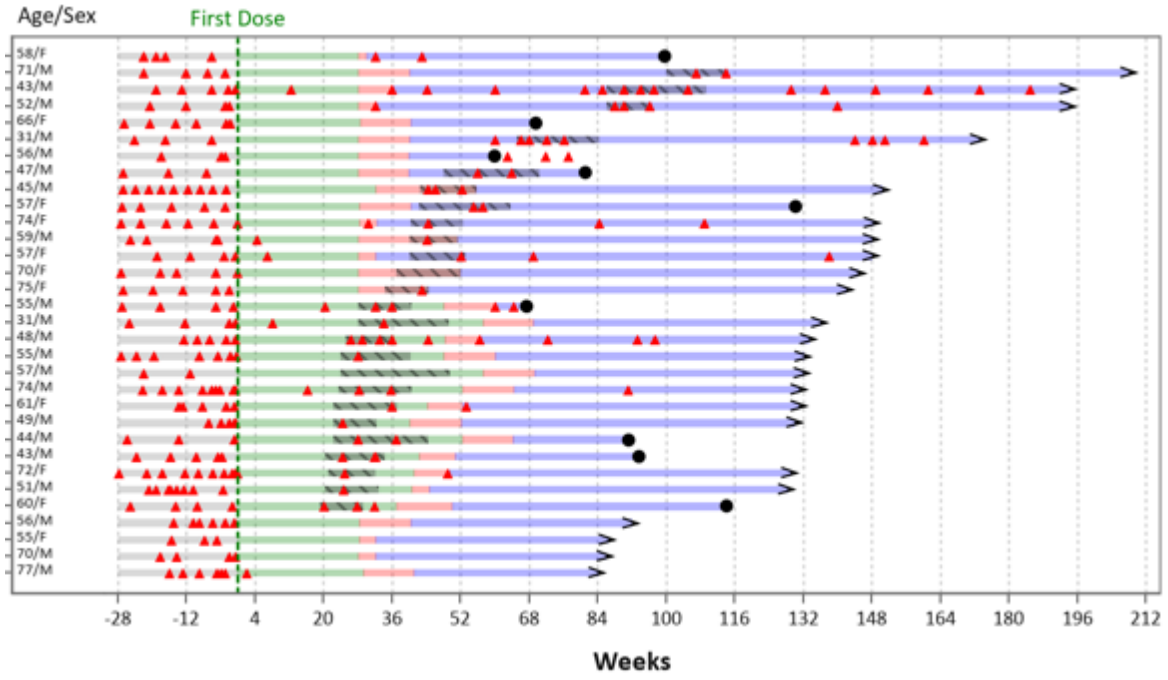
REVIVE: Durability of Rusfertide Efficacy

Significant Reduction in Therapeutic Phlebotomy

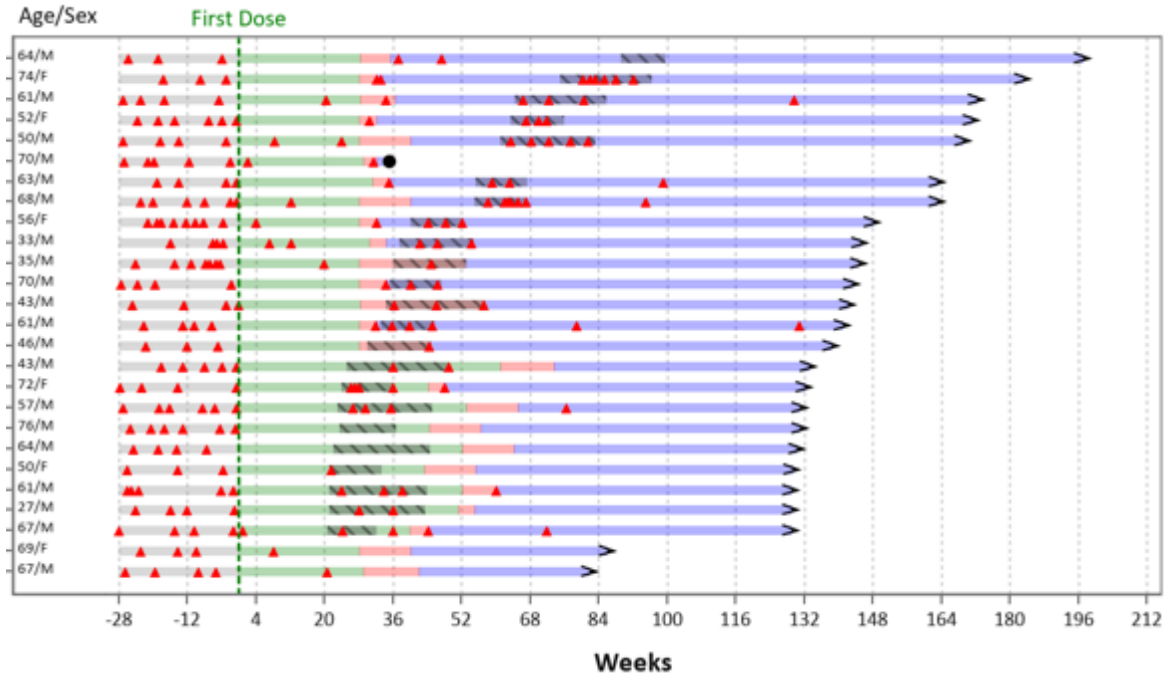
Ph2 REVIVE Study

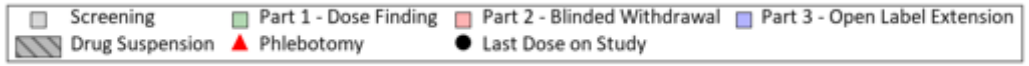
- In patients who continued onto Part 3, 32 (55.2%) and 26 (44.8%) patients were treated with phlebotomy alone or phlebotomy with cytoreductive therapy, respectively

Phlebotomy Only (n=32)



Phlebotomy + Cytoreductive Therapy (n=26)





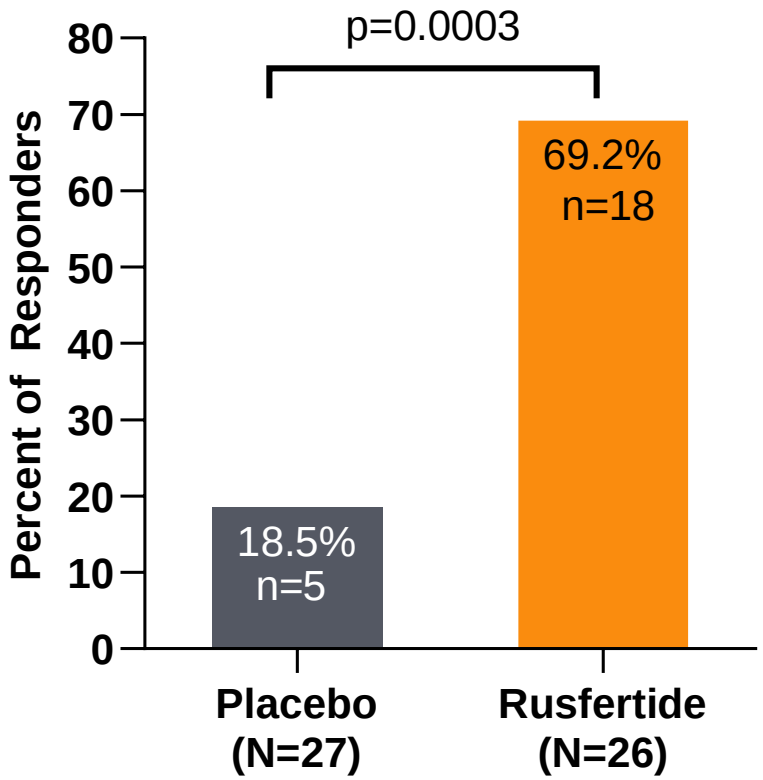
Protagonist Therapeutics

Adapted from Ritchie EK, et al. Durability of Hematocrit Control in Polycythemia Vera with the First-in-Class Hepcidin Mimetic Rusfertide: Two-Year Follow up Results from the Revive Study. *Blood*. 2023;142 (Supplement 1): 745.

Part 2: Blinded Randomized Withdrawal, Weeks 29-41

Rusfertide Met the Primary Endpoint of Efficacy (p=0.0003)

Highly Significant Efficacy*
in Rusfertide Arm vs. Placebo



- **69.2% subjects (18 out of 26) are responders. 8 non-responders as per protocol definition**
  - 3 fulfilled the phlebotomy eligibility criteria
  - 5 discontinued treatment per patient/investigator discretion
- **All 8 non-responders continued in the Part 3 open label extension part of the study**
  - 7 out of 8 are currently continuing treatment
- **92.3% subjects** (24 out of 26) in rusfertide arm did not receive phlebotomy in Part 2, the 12-week randomization part of the study

**Responder definition as per protocol*

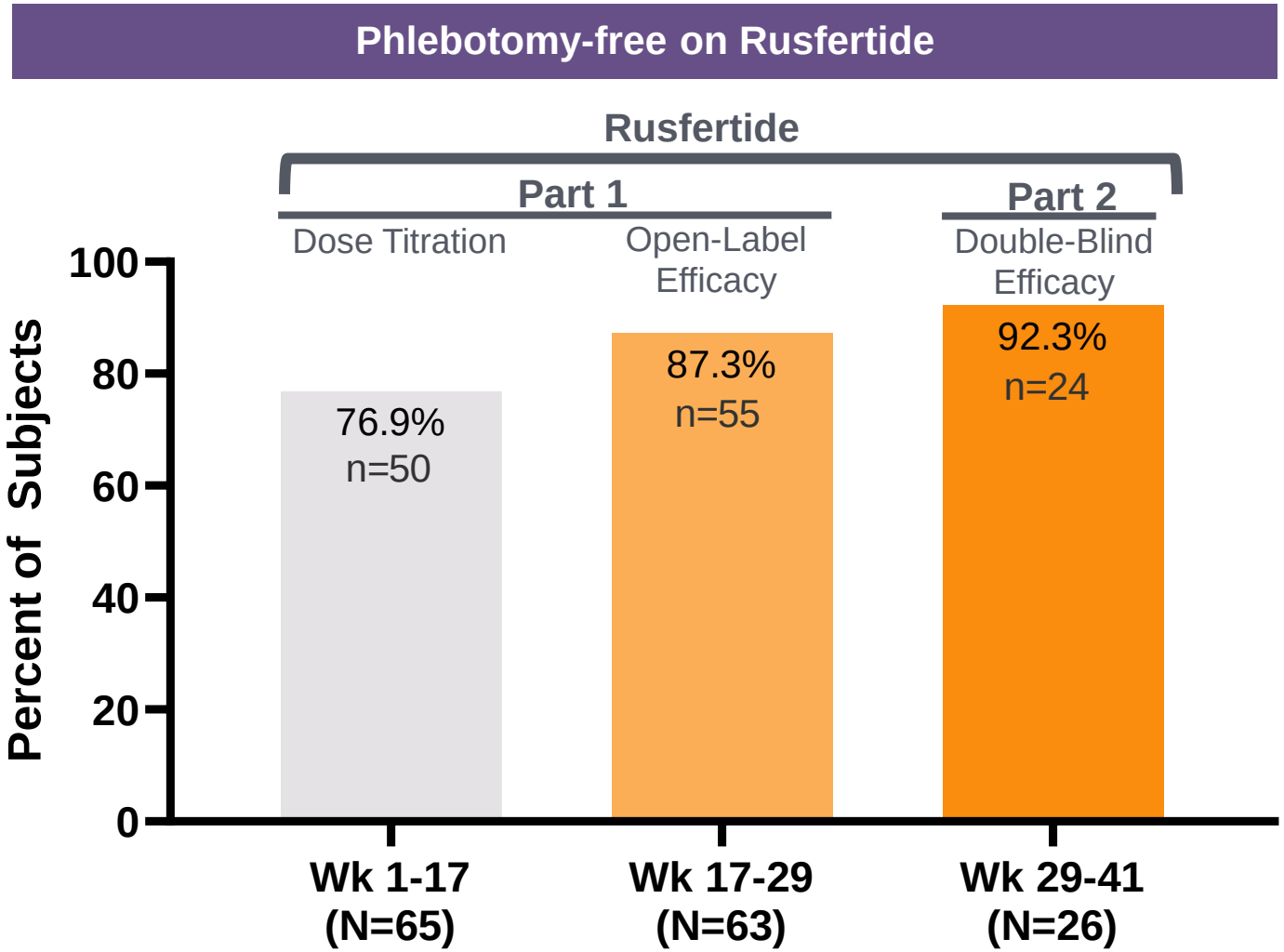
- *Did not receive a phlebotomy*
- *Completed 12 weeks of treatment*
- *Hematocrit control maintained without phlebotomy eligibility, which is defined as*
  - *Hematocrit ≥45% that was ≥3% higher than Week 29 pre-randomization hematocrit value **or***
  - *Hematocrit >48% **or***
  - *An increase of ≥5% in hematocrit compared to Week 29 pre-randomization hematocrit value*

Protagonist Therapeutics

Adapted from Kremyanskaya et al. EHA2023; Abstract LB2710.

Phase 2 REVIVE Study: Part 1 and 2

Consistent Effects on Freedom from Phlebotomy



Protagonist Therapeutics

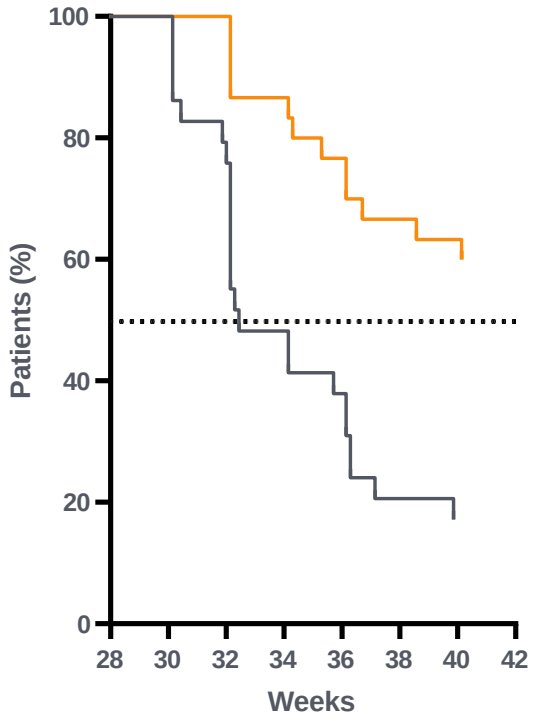
Adapted from Kuykendall A, et al. *HemaSphere.* 2023;7(S3):1934-5.

Phase 2 REVIVE Study: Time to Event Analysis

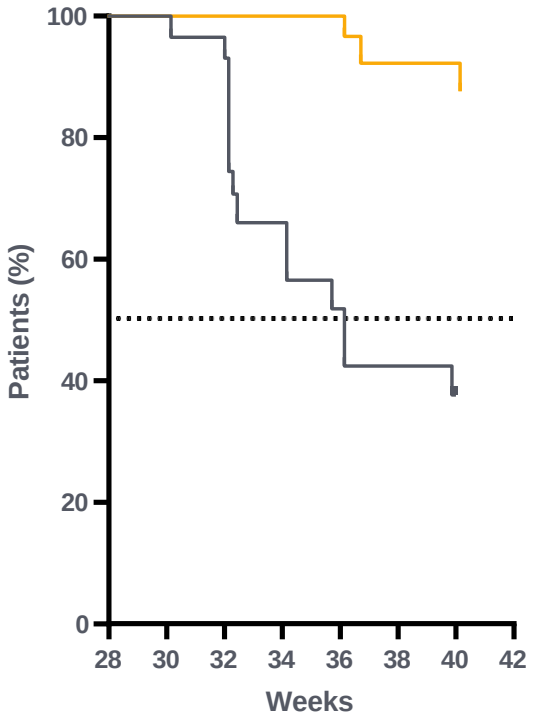
Rusfertide Associated With Delayed Time to Loss of Response, Phlebotomy Eligibility, and First Hct ≥45%

Ph2 REVIVE Study

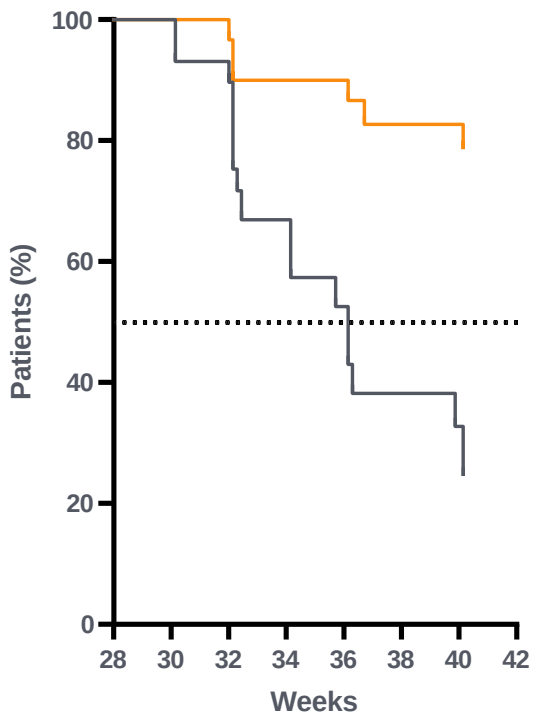
Time to Loss of Response



Time to Phlebotomy Eligibility



Time to First Hct ≥45%



Placebo (N=29)
Rusfertide (N=30)

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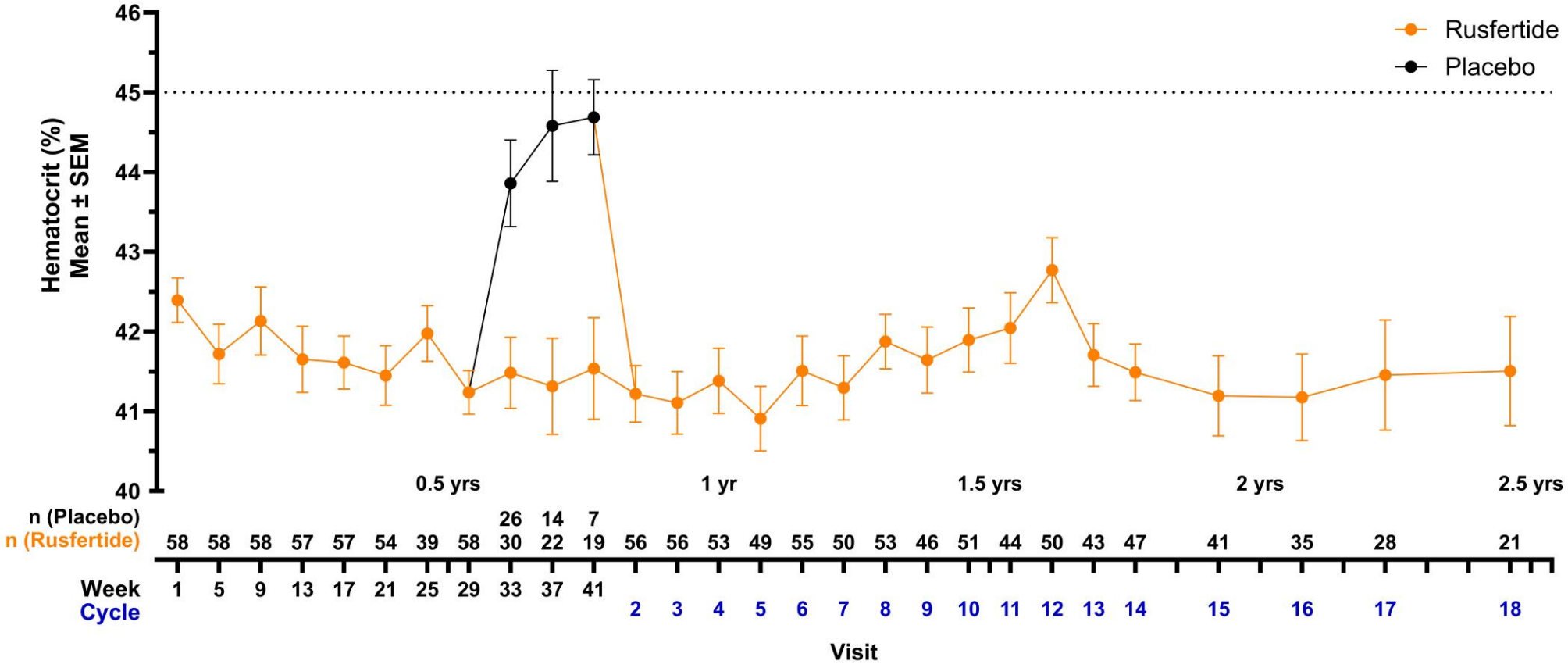
Protagonist Therapeutics, Inc. Data on File. 2 January 2024.

Rusfertide Provided Durable Control of Hematocrit Through 2.5 Years

REVIVE Part 3: Open-Label Extension (OLE)

Ph2 REVIVE Study



- Rusfertide treatment resulted in consistent maintenance of hematocrit <45%

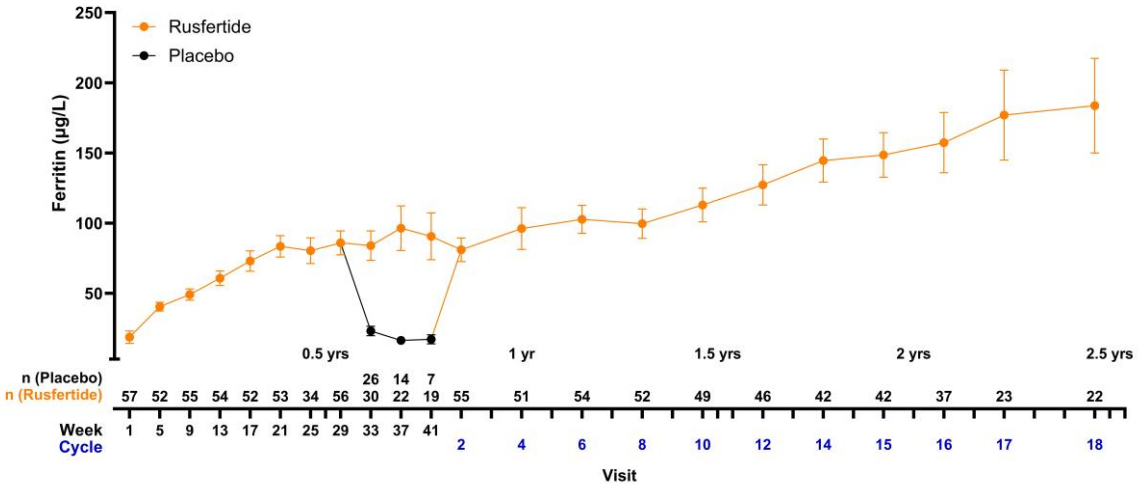
Protagonist Therapeutics

Adapted from Ritchie EK, et al. Durability of Hematocrit Control in Polycythemia Vera with the First-in-Class Hepcidin Mimetic Rusfertide: Two-Year Follow up Results from the Revive Study. *Blood*. 2023;142 (Supplement 1): 745.

Phase 2 REVIVE Study: Symptom Improvement

Improvement in Ferritin Levels and Symptoms

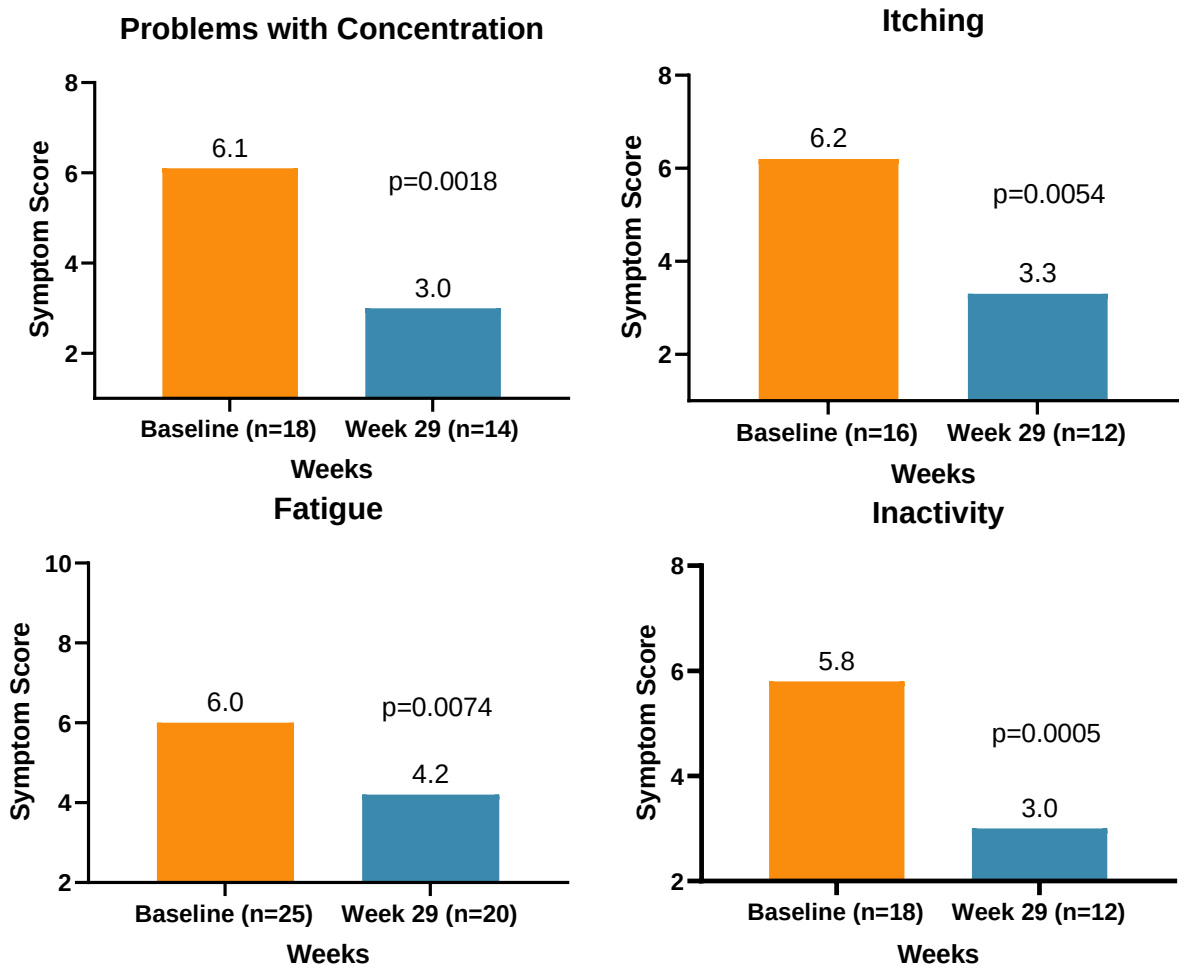
Serum Ferritin (Central) Data (Mean ± 1 SEM)[1]



- Prior to enrollment, iron-related parameters were consistent with systemic iron deficiency
- Rusfertide resulted in normalization of serum ferritin levels over 2.5 years

[1]Adapted from Ritchie EK, et al. Durability of Hematocrit Control in Polycythemia Vera with the First-in-Class Hepcidin Mimetic Rusfertide: Two-Year Follow up Results from the Revive Study. *Blood*. 2023;142 (Supplement 1): 745.

Symptom Improvements in Part 1 (28 Weeks)[2]



Individual symptoms assessed using MPN-SAF; p-values are based on paired comparisons

[2]Adapted from Kremyanskaya et al. EHA2023; Abstract LB2710.

Protagonist Therapeutics

Phase 2 REVIVE Study: Safety and Exposure

Rusfertide Was Generally Well Tolerated

Summary of Reported TEAEs (Any Grade) by Preferred Term Noted at ≥10%	N=70
Patients with at least 1 TEAE	70 (100.0)
Injection site erythema	46 (65.7)
Injection site pain	28 (40.0)
Injection site pruritus	28 (40.0)
Fatigue	23 (32.9)
Injection site mass	21 (30.0)
Arthralgia	19 (27.1)
Pruritus	19 (27.1)
Injection site swelling	18 (25.7)
COVID-19	17 (24.3)
Dizziness	17 (24.3)
Headache	16 (22.9)
Nausea	16 (22.9)
Anemia	15 (21.4)
Injection site irritation	14 (20.0)
Injection site bruising	11 (15.7)
Diarrhea	10 (14.3)
Dyspnea	10 (14.3)
Hyperhidrosis	10 (14.3)
Injection site warmth	10 (14.3)

- **70 subjects were enrolled in the rusfertide REVIVE study**
  - 57 subjects (81.4%) have exposure ≥ 1 yr
  - 51 subjects (72.9%) have exposure ≥ 1.5 yrs
  - 37 subjects (52.9%) have exposure ≥ 2 yrs
  - 11 subjects (15.7%) have exposure ≥ 2.5 yrs
  - 4 subjects (5.7%) have exposure ≥ 3 yrs
  - Overall, the median duration of exposure to rusfertide was 105.4 weeks (range, 3-182 weeks)
- **Rusfertide was generally well tolerated**
  - A majority of TEAEs were Grade 1 or 2
    - Overall, 77.1% of TEAEs had a maximum grade of 2
    - Overall, 21.4% of TEAEs were grade 3
    - No Grade 4 or 5 TEAEs
  - The most common TEAEs were injection site reactions, which were localized and grade 1-2 in severity and decreased in incidence

Protagonist Therapeutics

Adapted from Ritchie EK, et al. Durability of Hematocrit Control in Polycythemia Vera with the First-in-Class Hepcidin Mimetic Rusfertide: Two-Year Follow up Results from the Revive Study. *Blood*. 2023;142 (Supplement 1): 745.

Data as of 17 October 2023

REVIVE: Serious Adverse Events

No New Safety Signals

- Overall, 14 patients (20.0%) experienced an SAE*
  - There were 3 cases of basal cell carcinoma
  - There was 1 case each of atrial fibrillation, myocardial infarction, anogenital dysplasia, constipation, non-cardiac chest pain, gastroenteritis, sepsis, lung adenocarcinoma, malignant melanoma, malignant melanoma (Stage I), acute myeloid leukemia (Part 2; placebo arm), squamous cell carcinoma (Part 2; placebo arm), ischemic stroke, syncope, transient ischemic attack, peripheral artery aneurysm, and peripheral vascular disorder
- The nature of the SAEs observed is consistent with comorbidities anticipated in the PV population, including vascular events and skin cancer

**Most SAEs were assessed as being unrelated to rusfertide by the investigators*

Data cutoff: 17 October 2023

PV, polycythemia vera; SAE, serious adverse event.

Adapted from Ritchie EK, et al. Durability of Hematocrit Control in Polycythemia Vera with the First-in-Class Hepcidin Mimetic Rusfertide: Two-Year Follow up Results from the Revive Study. *Blood*. 2023;142 (Supplement 1): 745.

Prevalence of Second Cancers in PV

Second Cancers

- One large population-based study found that **patients with MPNs had a 60% higher risk of developing second non-hematologic cancers** compared to matched controls[1]
  - **Skin cancers were among the most prevalent second cancers** (2.8-fold increase in risk of non-melanoma skin cancer vs. matched controls)
- In a retrospective analysis of US electronic health records contained in the Optum® MarketClarity database, the post-index period prevalence of second cancers was evaluated in 20,000+ PV patients (date range: 2007-2019)[2]
  - **35.7%** of patients had **at least one second cancer** in the post-index period; **the highest rates were observed for skin cancers**
    - **9.1%** of patients had **any form of skin cancer**
    - **8.3%** of patients had **non-melanoma skin cancer**
    - **1.4%** of patients had **melanoma**
  - Patients treated with hydroxyurea had nearly **2×** the rate of skin cancers compared to patients treated with phlebotomy alone
- **Given these data[1,2], patients with PV appear to have high rates of second cancers, including skin cancers**

Protagonist Therapeutics

MPN, myeloproliferative neoplasm; PV, polycythemia vera; TE, thromboembolic event.

1. Landtblom AR, et al. *Leukemia*. 2018;32:2203-10. 2. Pemmaraju N, et al., *Blood* 2023; 142 (Supplement 1): 3190.

Rusfertide Summary

An Investigational Injectable Hepcidin Mimetic for Treatment of Polycythemia Vera

- **PV patients requiring frequent phlebotomy ± cytoreductives have been treated with rusfertide for *>2 years* in the REVIVE study, with subjects remaining essentially phlebotomy free**
  - Rapid, sustained and durable hematocrit control
  - Robust efficacy in all categories of patients
  - Rusfertide dosing was interrupted and led to loss of effect; restart restored therapeutic benefits
  - Positive improvements in symptom scores
  - 53 patients, 1:1 randomization part 2 of the study completed

- **Rapid Hct control (<45%) without phlebotomy in high Hct (>48%) PACIFIC study**

- **Rusfertide treatment with or without cytoreductives appears to be well tolerated**
  - Safety update presented at ASH in December 2023; no new safety signals observed[1]

- **~250 patient, randomized, placebo-controlled Ph3 VERIFY study to confirm efficacy and safety**
  - Execution underway, enrollment completion by 1Q 2024

Protagonist Therapeutics

1. Pemmaraju, Naveen, et al. "Subgroup Analysis of Adverse Events Following Rusfertide Dosing in Revive: A Phase 2 Study of Patients with Polycythemia Vera." *Blood* 140.Supplement 1 (2022): 6835-6837.

Phase 3 Study **VERIFY** (NCT05210790): Rusfertide vs Placebo in Patients With PV

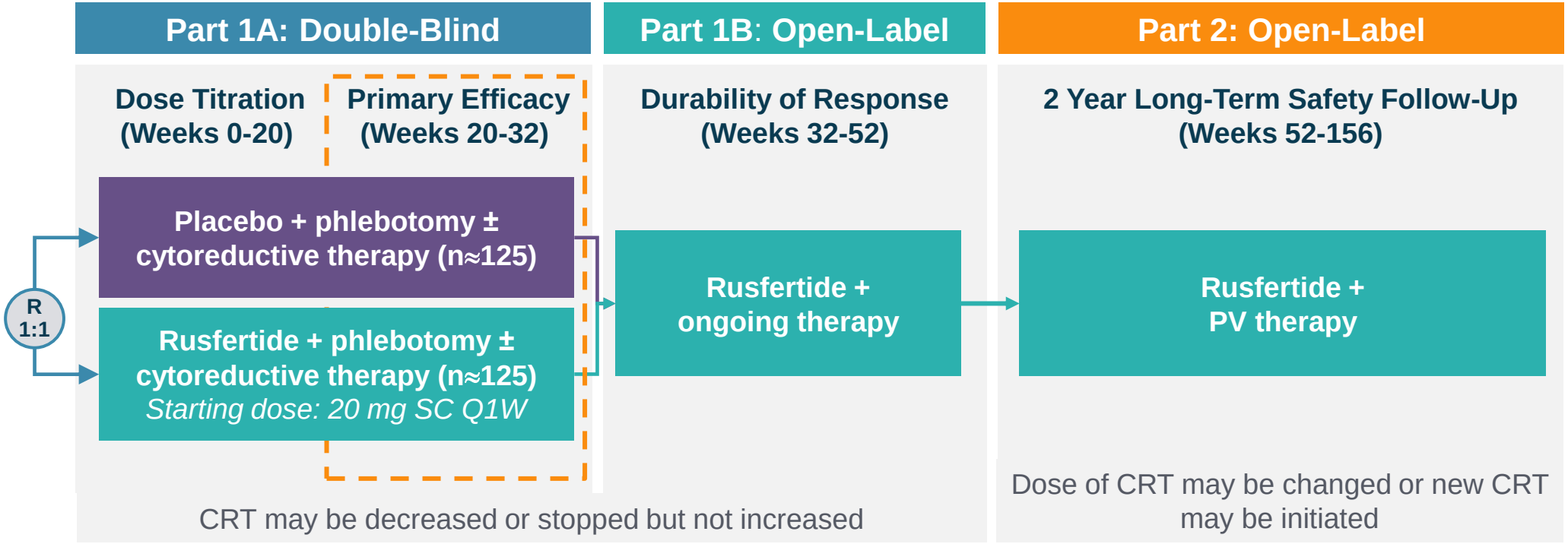
Pathway to Potential Registration in the USA and Europe

Phase 3 VERIFY study design capitalizes on the successful outcome to date of the Phase 2 REVIVE Study

Key Eligibility:

- Age ≥18 years
- Meet revised 2016 WHO criteria for diagnosis of PV
- ≥3 phlebotomies due to inadequate Hct control in 28 weeks before randomization OR ≥5 phlebotomies due to inadequate Hct control within 1 year prior to randomization

N≈250



Key Endpoints:

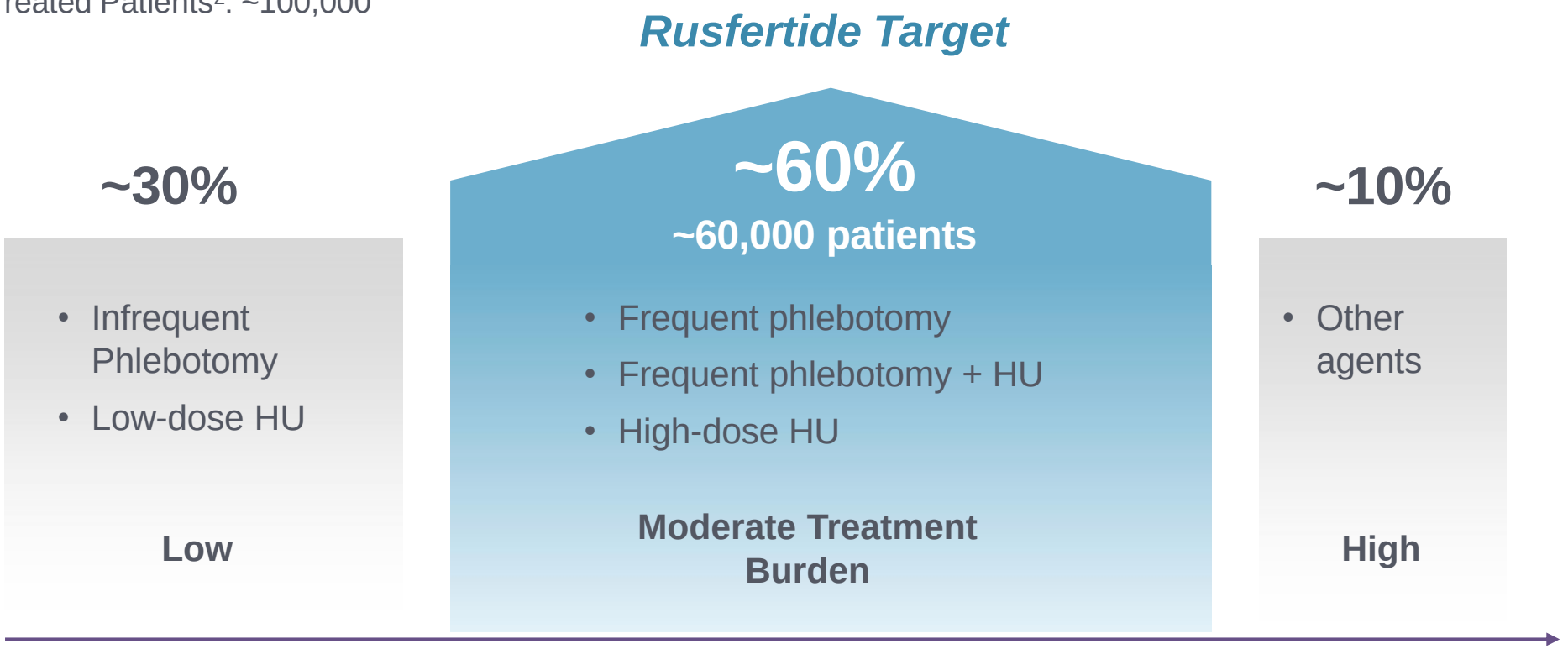
- Proportion of patients achieving response (defined as absence of phlebotomy eligibility; measured between Weeks 20-32)
- Mean number of phlebotomies (Weeks 0-32)

Protagonist Therapeutics

Potential Commercial Positioning for Rusfertide

Potential Therapy of Choice for Patients with Moderate Treatment Burden

Prevalent Patients in US[1]: ~160,000
Diagnosed & Treated Patients[2]: ~100,000



1. Based on NORD estimates (44 to 57 per 100,000 people in the US) 2. Internal estimates based on data on file Komodo claims data 2016-2022. Symphony claims data 2019-2021.

Clinical Study of Rusfertide in Patients with Hemochromatosis

Control Serum Iron and Reduce Phlebotomies

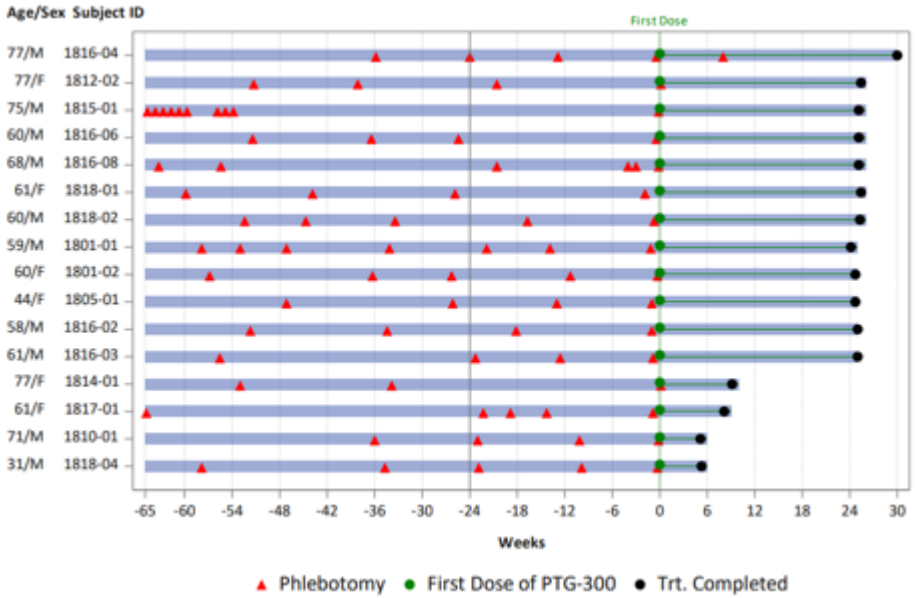
Ph2 PoC Study

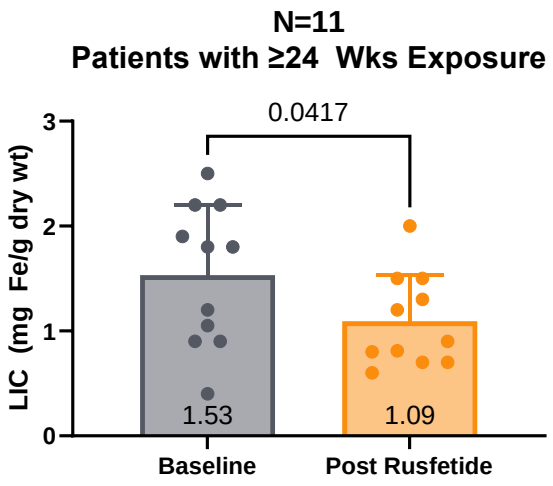
- **Open-label, 24-week proof-of-concept study in patients with hemochromatosis**

- **Eligibility**
  - Adults with HFE-related hemochromatosis.
  - History of ≥3 phlebotomies in 12 months or ≥4 phlebotomies in 15 months

- **Clinical endpoints**
  - Number of phlebotomies
  - Liver Iron Concentration (LIC) by MRI

- **Manuscript published in *Lancet Gastroenterol Hepatol* in December 2023[1]**
  - Rusfertide treatment rapidly reduced and suppressed serum iron and TSAT.
  - Essential elimination of phlebotomies and stable LIC.
  - Rusfertide was generally well tolerated





1. Kowdley KV, et al. Rusfertide for the treatment of iron overload in HFE-related haemochromatosis: an open-label, multicentre, proof-of-concept phase 2 trial. *Lancet Gastroenterol Hepatol*. 2023;8(12):1118-28.

Protagonist Therapeutics

JNJ-2113: Oral IL-23 Receptor Antagonist Peptide

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

Protagonist-Janssen Oral, IL-23R Antagonist Collaboration

Collaboration overview

- Initiated in 2017 with I&I market leader Janssen Biotech[1]
- JNJ-2113 (formerly PN-235) jointly discovered using Protagonist's proprietary peptide discovery platform
  - Protagonist completed pre-clinical and first Phase 1 study
  - Janssen responsible for further development and commercialization

Comprehensive JNJ-2113 Phase 3 registrational program (ICONIC) in psoriasis

- Four Phase 3 studies
- PASI 90 highlighted as high-bar primary endpoint to reflect the modern clinical goal of durable, symptom-free remission
- Two head-to-head trials vs. deucravacitinib
- All psoriasis trials to be conducted with single dose of JNJ-2113 at 200 mg once-daily

Phase 2b study in ulcerative colitis ongoing (ANTHEM)

JNJ-2113 highlighted as first- and best-in class targeted oral IL-23 peptide antagonist[2]

- "Unprecedented potential" from JNJ-2113 across multiple indications: IBD, plaque psoriasis, psoriatic arthritis, IBD
- PTGX positioned as delivering "transformational science" and a source or "best innovation" alongside two other JNJ partners
- "Potential peak year sales for JNJ-2113 across indications: $5B+"

Protagonist Therapeutics

1. Stelara® generated $9.7B in sales, and Tremfya® generated $2.7B in sales in 2022, per Johnson & Johnson 2022 Annual Report. Stelara® and Tremfaya® not part of Protagonist-Janssen collaboration. 2. JNJ Innovative Medicines Enterprise Business Review, Dec 5, 2023.

JNJ-2113 Market Potential[1]

Big Opportunity for a safe and effective oral, once daily medication

- 50-70% of patients (~5 million in G8) living with psoriatic and IBD conditions and are eligible for advanced therapies, and yet aren't receiving them

Reasons eligible patients avoid using advanced treatments[2]

30% Method of administration

75% Overall risk/ benefit profile

Market growth expected to be driven by orals[4]

Patients on injectables who would switch to an oral with similar safety & efficacy[3] 75%

~5M Eligible patients not receiving advanced therapy

Growing Market for Oral Treatment Options[5]

WW market Size 2030 est. (7-yr CAGR)[1]

PsO	~$35B (4-6%)
PsA	~$8B (4-6%)
CD	~$19B (2-4%)
UC	~$13B (7-9%)

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. EvaluatePharma WW Sales by Indication Sep 2023 extrapolated 2028-30

Protagonist Therapeutics

JNJ-2113: Oral, IL-23R Peptide Antagonist

Preclinical, Phase 1 and Phase 2b Data Supportive of a Robust Clinical Development Program[1]

Highly Potent Oral IL-23R Antagonist	High Oral Stability	Pre-clinical Proof-of-Concept	Phase 1 studies in NHVs	Phase 2b FRONTIER1 study in Psoriasis
• **Picomolar potency** Similar or better target affinity vs. IL-23 mAbs	• >24hr half-life in feces (human, cyno, and rat) • >25% fecal recovery after 24hrs in cynos	• Rat ear skin inflammation model • Rat TNBS colitis model	• PD based PoC: Inhibition of IL-23 biomarkers	• Potential for best-in-class oral agent for psoriasis

Protagonist – JNJ Innovative Medicines Discovery & Development Partnership

1. ISID – Fourie A, et al. First-in-Class Oral Peptide Systemically Targeting the IL-23 Pathway. Abstract presented at the International Societies for Investigative Dermatology; May 2023
WCD – Bissonnette R, et al. A Phase 2, Randomized, Placebo-controlled, Dose Ranging Study of Oral JNJ-77242113 for the Treatment of Moderate-to-Severe Plaque Psoriasis: FRONTIER 1. Late Breaking Abstract presented at the World Congress of Dermatology; July 2023

Protagonist Therapeutics

JNJ-2113 FRONTIER 1 Phase 2b Plaque Psoriasis (PsO) Study

A Phase 2b multicenter, randomized, placebo controlled, dose-ranging study to evaluate the efficacy and safety of JNJ-2113 for the treatment of moderate-to-severe plaque psoriasis

Adult Patients with PP

N=255

Eligibility

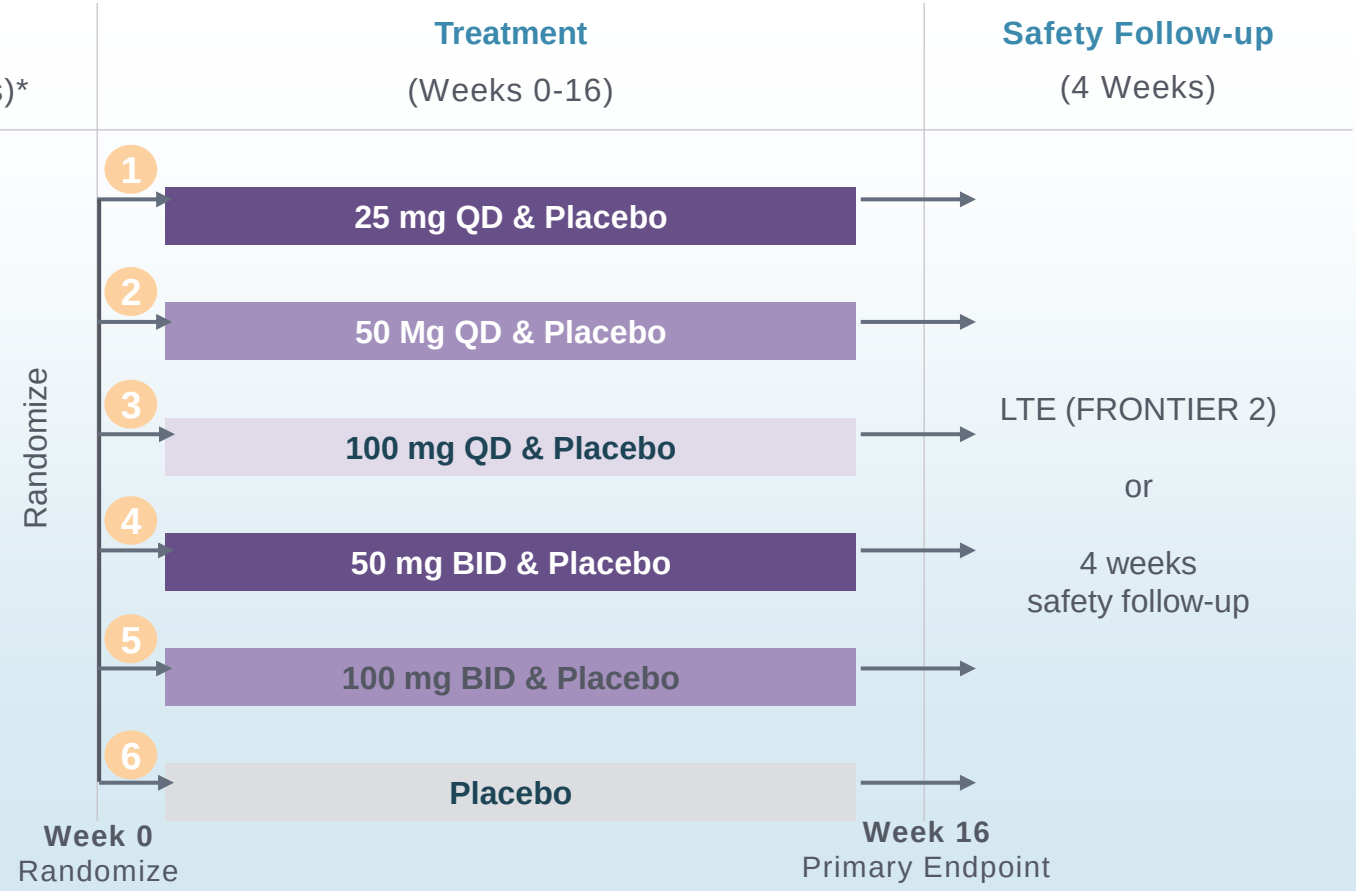
- Moderate – Severe PP

Inclusion

- BSA ≥ 10%
- PASI ≥ 12

Primary endpoint

- PASI ≥ 75 at Week 16



Protagonist Therapeutics

Demographics and Disease Characteristics at Baseline

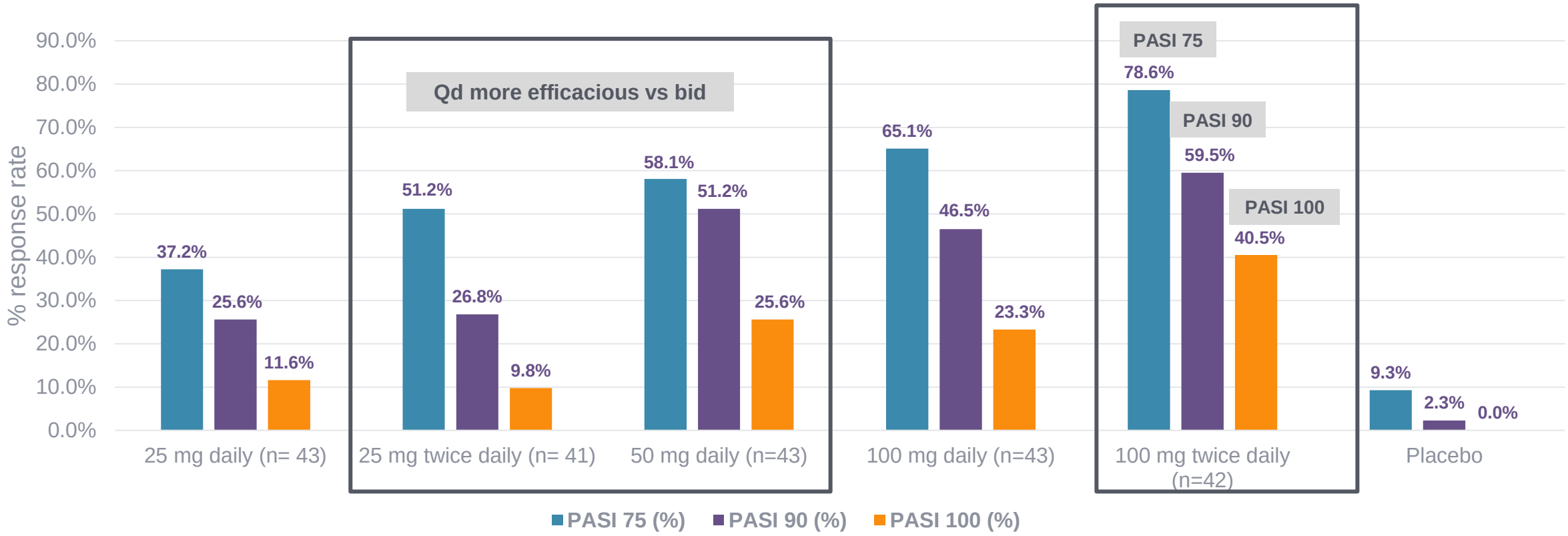
	Placebo	JNJ-77242113						Total
		25 mg QD	50 mg QD	25 mg BID	100 mg QD	100 mg BID	Combined*	
Full analysis set	43	43	43	41	43	42	212	255
Age (yrs)	43.9 (14.70)	44.5 (12.72)	45.1 (11.08)	45.7 (11.91)	44.7 (14.11)	42.0 (11.34)	44.4 (12.24)	44.3 (12.65)
Weight (kg)	92.1 (24.66)	89.0 (19.42)	87.6 (19.23)	90.8 (22.12)	85.4 (22.49)	88.5 (16.94)	88.2 (20.03)	88.9 (20.87)
BMI (kg/m²)	31.2 (7.61)	30.0 (7.25)	29.3 (5.97)	30.2 (6.72)	28.8 (7.39)	30.0 (5.40)	29.6 (6.55)	29.9 (6.75)
PsO disease duration (yrs)	17.9 (14.37)	15.5 (11.76)	21.5 (11.16)	18.1 (11.82)	19.5 (13.34)	16.7 (13.78)	18.3 (12.48)	18.2 (12.79)
Age at diagnosis (yrs)	26.1 (15.55)	29.1 (15.56)	23.7 (11.57)	27.7 (13.73)	25.3 (15.08)	25.5 (15.26)	26.2 (14.31)	26.2 (14.50)
PASI total score	18.99 (5.341)	18.90 (5.272)	19.23 (5.082)	18.46 (5.838)	18.42 (6.873)	20.33 (6.509)	19.07 (5.938)	19.05 (5.831)
IGA score, n (%)								
Severe (4)	5 (11.6%)	13 (30.2%)	7 (16.3%)	8 (19.5%)	8 (18.6%)	12 (28.6%)	48 (22.6%)	53 (20.8%)
Moderate (3)	38 (88.4%)	30 (69.8%)	36 (83.7%)	33 (80.5%)	35 (81.4%)	30 (71.4%)	164 (77.4%)	202 (79.2%)
Previous Psoriasis Medications/Therapies, n (%)								
Phototherapy**	19 (44.2%)	17 (39.5%)	24 (55.8%)	15 (36.6%)	21 (48.8%)	14 (33.3%)	91 (42.9%)	110 (43.1%)
Biologics†	7 (16.3%)	7 (16.3%)	11 (25.6%)	13 (31.7%)	9 (20.9%)	9 (21.4%)	49 (23.1%)	56 (22.0%)
Systemics‡	34 (79.1%)	33 (76.7%)	35 (81.4%)	33 (80.5%)	34 (79.1%)	31 (73.8%)	166 (78.3%)	200 (78.4%)

BID=Twice daily; BMI=Body mass index; IGA=Investigator's Global Assessment; PASI=Psoriasis Area and Severity Index; PsO=Psoriasis; PUVA=Psoralen plus ultraviolet A; QD=Daily; UVB=Ultraviolet B. Data shown are mean (SD), unless otherwise indicated. *Includes all JNJ-77242113 treatment columns. **Includes PUVA or UVB. †Includes etanercept, infliximab, adalimumab, ustekinumab, briakinumab, secukinumab, ixekizumab, brodalumab, guselkumab, risankizumab, tildrakizumab, alefacept, efalizumab, natalizumab, certolizumab pegol. ‡Includes conventional nonbiologic systemics, novel nonbiologic systemics, 1,25-vitamin D3 and analogues, phototherapy, biologics.

Protagonist Therapeutics

JNJ-2113 Phase 2B Frontier 1 Data

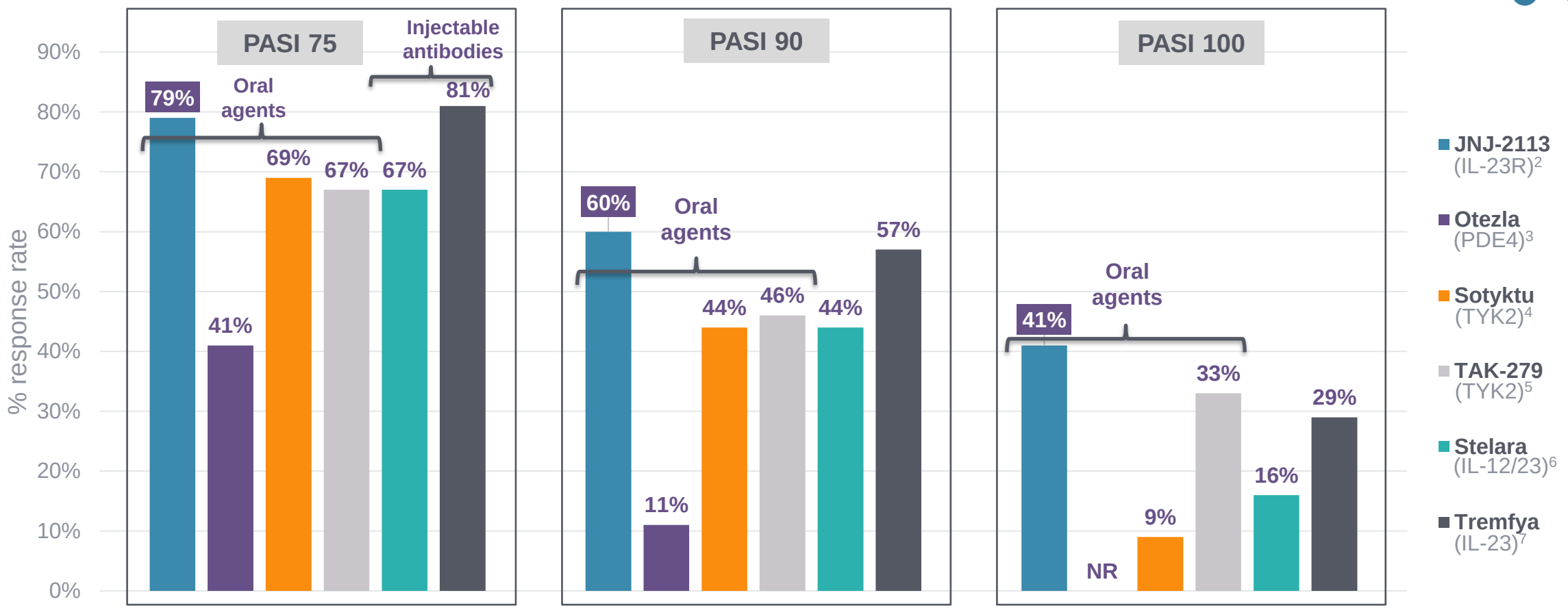
Dose Response



- **200 mg once daily oral dose selected for all four phase 3 psoriasis studies**
- **PASI 90 as a high-bar primary endpoint in these phase 3 studies**

Protagonist Therapeutics

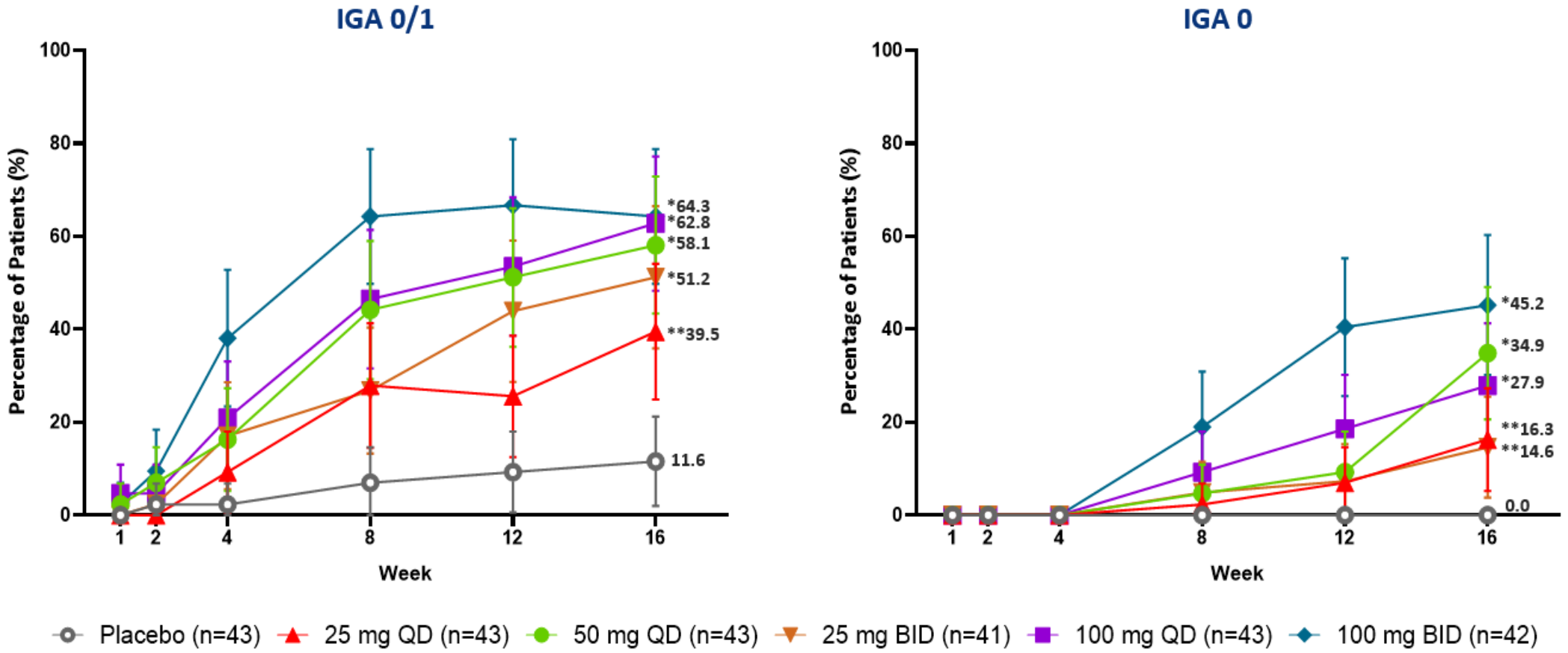
Cross-Study Comparison of JNJ-2113 to Clinically Relevant Phase 2 Benchmarks[1]



1. Cross trial (not head-to-head) comparisons
2. JNJ2113 100 mg bid dose. Wk 16 endpoint (Placebo: PASI 75: 9.3%, PASI 90: 2.3%, PASI 100: 0%)
3. Otezla 30 mg qd approved dose. Week 16 primary endpoint. Papp K et al. Lancet 2012; 380: 738–46. (Placebo: PASI 75: 5.7%, PASI 90: 1.1%, PASI 100: NR)
4. Sotyktu 3 mg bid dose (6 mg qd dose approved). Wk 12 primary endpoint. Papp K et al. N Engl J Med 2018; 379:1313-1321. (Placebo: PASI 75: 7%, PASI 90: 2%, PASI 100: 0%)
5. TAK-279 30 mg qd dose (Expected phase 3 dose). Wk 12 primary endpoint. AAD 2023. (Placebo: PASI 75: 5.8%, PASI 90: 0%, PASI 100: 0%)
6. Stelara 45 mg wkly x 4 (~approved 90 mg week 0 and 2 approved dose). Wk 12 primary endpoint. Krueger et al. N Engl J Med 2007;356:580-92. (Placebo: PASI 75: 2%, PASI 90: 2%, PASI 100: 0%)
7. Tremfya 200 mg wk 0, 4, then q 8 wks (approved dose 100 mg wk 0, 4 then q 8 wks). Wk 16 primary endpoint. Gordon KB et al. N Engl J Med 2015;373:136-44. (Placebo: PASI 75: 5%, PASI 90: 2%, PASI 100: 0%)

Protagonist Therapeutics

Proportion of Patients Achieving IGA 0/1 and IGA 0 (95% CI) Through Week 16



Non-responder imputation

*nominal p <0.001 vs placebo; **nominal p<0.01 vs placebo. p-values are based on Cochran-Mantel-Haenszel (CMH) chi-square test stratified by baseline weight category (≤90 kg, >90 kg). Patients who discontinued study agent due to lack of efficacy/worsening of PsO, or who initiated a prohibited PsO treatment were considered non-responders after the occurrence. Patients with missing data were considered non-responders.

Protagonist Therapeutics

Number of Patients With ≥1 TEAE With Frequency of ≥5% of Preferred Terms in Any Treatment Group Through End of Study by System Organ Class and Preferred Term

	Placebo	JNJ-77242113					
		25 mg QD	50 mg QD	25 mg BID	100 mg QD	100 mg BID	Combined*
Safety analysis set, n	43	43	43	41	43	42	212
Avg duration of follow-up (weeks)	15.03	15.70	15.75	16.20	16.07	15.81	15.90
Patients with ≥1 AE, n (%)	22 (51.2%)	20 (46.5%)	26 (60.5%)	20 (48.8%)	19 (44.2%)	26 (61.9%)	111 (52.4%)
System organ class/Preferred term, n (%)							
Infections and infestations	12 (27.9%)	15 (34.9%)	17 (39.5%)	14 (34.1%)	7 (16.3%)	11 (26.2%)	64 (30.2%)
COVID-19	5 (11.6%)	5 (11.6%)	3 (7.0%)	8 (19.5%)	3 (7.0%)	4 (9.5%)	23 (10.8%)
Nasopharyngitis	2 (4.7%)	1 (2.3%)	8 (18.6%)	3 (7.3%)	1 (2.3%)	2 (4.8%)	15 (7.1%)
Upper respiratory tract infection	1 (2.3%)	3 (7.0%)	0	0	0	2 (4.8%)	5 (2.4%)
Gastrointestinal disorders	5 (11.6%)	3 (7.0%)	6 (14.0%)	4 (9.8%)	4 (9.3%)	7 (16.7%)	24 (11.3%)
Diarrhoea	1 (2.3%)	2 (4.7%)	4 (9.3%)	2 (4.9%)	1 (2.3%)	1 (2.4%)	10 (4.7%)
Nervous system disorders	1 (2.3%)	0	3 (7.0%)	2 (4.9%)	3 (7.0%)	2 (4.8%)	10 (4.7%)
Headache	1 (2.3%)	0	1 (2.3%)	1 (2.4%)	3 (7.0%)	1 (2.4%)	6 (2.8%)
Respiratory, thoracic and mediastinal disorders	1 (2.3%)	1 (2.3%)	1 (2.3%)	0	3 (7.0%)	2 (4.8%)	7 (3.3%)
Cough	0	1 (2.3%)	1 (2.3%)	0	3 (7.0%)	1 (2.4%)	6 (2.8%)

AE=Adverse event; BID=Twice daily; QD=Daily; TEAE=Treatment-Emergent Adverse Events. *Includes all JNJ-2113 treatment columns.
Patients are counted only once for any given event, regardless of the number of times they actually experienced the event. Adverse events are coded using MedDRA Version 25.1.

Protagonist Therapeutics

JNJ-2113 FRONTIER 1 Phase 2b Plaque Psoriasis (PsO) Study

Safety Summary

The proportion of patients experiencing 1 or more AEs was comparable between JNJ-77242113 groups and the placebo group

- Most frequently reported AEs were COVID-19 and nasopharyngitis
- There was no evidence of dose-dependent increase in the occurrence of AEs across the JNJ-77242113 treatment groups

There were three serious AEs that occurred in FRONTIER-1 (n=1 each: suicide attempt, COVID-19, infected cyst; all on active drug and assessed as not related to study intervention by investigators).

No dose-dependent relationship was observed.

A low number of laboratory abnormalities occurred during the study and were comparable between placebo and JNJ-77242113 groups.

There was no evidence of a dose-dependent increase in the occurrence of abnormalities.

There were no deaths, MACE, or malignancies during the study.

Protagonist Therapeutics

JNJ-2113 (formerly PN-235)

Conclusions from Phase 2b Psoriasis Study and Next Steps

Innovation

- Oral IL-23R antagonist peptide
- First-in-class
- Only-in-class
- Efficacious, well-tolerated

Efficacy

- Statistically significant efficacy vs. placebo across all doses
- A dose-response in PASI scores (75, 90, 100)

Safety

- Well tolerated at all doses with AEs comparable vs. placebo
- No dose dependent relationship in AEs

Potential

- Potential for best-in-class oral agent

Next Steps

- Further development in psoriasis and other IL-23 mediated disease indications is warranted

Next Steps

- Registrational program (ICONIC) with four phase 3 studies in psoriasis
  - Two head-to-head trials with deucravacitinib
- PASI 90 highlighted as a high-bar primary endpoint
- **200 mg oral once-daily dosing in all four phase 3 studies**

JNJ-2113 is a potential best, first-, and only-in-class oral IL-23 receptor antagonist

Protagonist Therapeutics

Publication in NEJM, 2024

- Patients were randomized to doses of 25 mg qd, 25 mg bid, 50 mg qd, 100 mg qd, or 100 mg bid or placebo
- Results demonstrate a dose-dependent Psoriasis Area and Severity Index score (PASI-75) response in patients treated with JNJ-2113 versus placebo at Week 16 (primary endpoint), with 79% of patients achieving a PASI-75 response in the highest dose group (100 mg twice daily)
- Secondary endpoints results consistent with primary evaluation
  - Highest dose of JNJ-2113 showed 59.5% of patients achieving PASI-90, and 40.5% of patients achieving a PASI-100 at Week 16
  - At the highest dose, 64.3% of patients achieved an Investigator Global Assessment (IGA) score of 0/1 and 45.2% of patients achieved a score of 0, with IGA responses showing separation between JNJ-2113 and placebo groups as early as Week 4
  - Significant improvements were observed across key Patient-Reported Outcomes
- JNJ-2113 is currently being studied in
  - the ICONIC program, which includes four Phase 3 studies for moderate-to-severe psoriasis
  - ANTHEM-UC, phase 2b study in moderate-to-severe ulcerative colitis

Results of FRONTIER-1 Phase 2b Study

JNJ-2113

Multiple Clinical Studies with Multiple Shots on Goal

Study	Phase 1	Phase 2	Phase 3	Key Milestones
NCT04621630	Ph1 in NHVs			• NHVs in Australia; completed
NCT05062200	Ph1 in NHVs			• Adult Japanese/Chinese participants; completed
NCT05703841	Ph1 in NHVs			• Healthy adult Chinese participants; completed
FRONTIER 1	Ph2b in Psoriasis, n~255			• Completed
FRONTIER 2	Ph2b in Psoriasis			• Delayed release formulation; completed
SUMMIT	Ph2a in Psoriasis, n~90			• Completed
ICONIC-LEAD	Ph3 in Psoriasis, n~600			• PASI 90 & IGA 0/1; completion ~Nov ’24*
ICONIC-TOTAL	Ph3 in Psoriasis, n~300			• Special areas IGA 0/1; completion ~Nov ’24*
ICONIC-ADVANCE 1	Ph3 in Psoriasis, n~750 pts			• Superiority study vs. deucravacitinib; completion ~Mar ‘25
ICONIC-ADVANCE 2	Ph3 in Psoriasis, n~675 pts			• Superiority study vs. deucravacitinib; completion ~Apr ‘25
ANTHEM-UC	Ph2b in UC, n~240 Pts			• Completion ~May ‘25

Protagonist Therapeutics

janssen

Milestones Status and Outlook

2024 and Beyond

$172.5M*

in upfront and development milestones have been achieved

$795M

amount of total future development and sales milestones for which Protagonist remains eligible

Royalty

6% to 10%

upward tiering

10% at ≥ $4B net sales

Upcoming Potential Milestones		
1st indication	Ph3 1° end point achieved	**$115M****
	NDA filing	**$35M****
	NDA approval	**$50M****
2nd indication	Ph3 initiation	**$15M****

***** Includes $60 million in milestones achieved in Q4 2023

**** $215M potential milestones NOT included in current cash runway forecast**

Protagonist Therapeutics

Protagonist Therapeutics

Discovery Pipeline Financial Outlook

2024 is a year of pipeline execution and strategic evolution for Protagonist

Discovery Pipeline

Leveraging Our Successes to Address Major Unmet Medical Needs and Create Value

Focus Areas			Strategic Rationale
	Lead Optimization	*Dev Candidate Nomination*	
I & I Inflammatory & Immunomodulatory Diseases	1H 2024	2H 2024	• Leverage the success of JNJ-2113 • Next generation oral peptides with best-in-class efficacy/safety in systemic immune-mediated diseases • Validated clinical targets • Internal expertise/experience to move in competitive disease areas with strong differentiation
Hematology Myeloproliferative Neoplasms	1H 2024	2H 2024	• Leverage end-to-end expertise in MPNs • Build upon rusfertide MPN commercial franchise • Address unmet medical needs in MPNs; moving beyond rusfertide • Oral and/or parenteral routes of administration

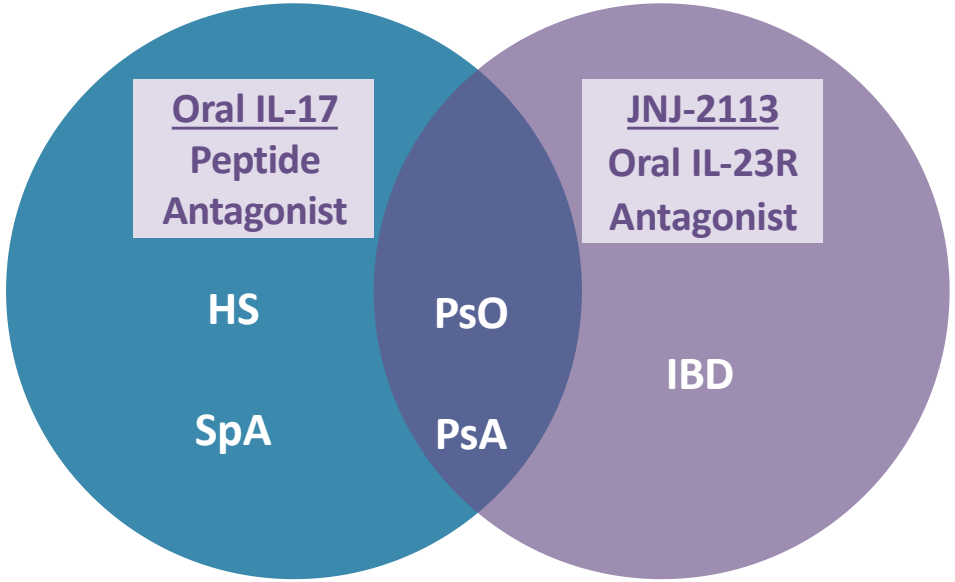
Oral IL-17 Peptide Antagonists

Protagonist Therapeutics

Oral IL-17 Peptide Antagonists

New Discovery Program

- IL-17 inhibitors expected to lead the I&I space
  - Global sales expected to increase significantly from ~$29B (2021) to >$50B (2031) for IL-17 mediated indications[1]
  - IL-23 and IL-17 inhibitors expected to have significant PsO (~80%) and PsA (~60%) market share by ~2035[2]
- Leveraging our oral peptide technology platform
- Target product profile (TPP)
  - Oral peptide, first-in-class
  - Similar/better potency vs. approved mAbs[3]
  - Tri-specific (IL-17 AA, AF & FF)
- Development candidate in 2024[4]



HS: Hidradenitis Suppurativa
SpA: Spondyloarthritis
PsO: Plaque Psoriasis
PsA: Psoriatic Arthritis
IBD: Inflammatory Bowel Diseases (Crohn's and Ulcerative Colitis)

Protagonist Therapeutics

1. JNJ Innovative Medicines Enterprise Business Review, Dec 5th, 2023 and Clarivate DRG Disease Landscape and Forecast; 2. JNJ Innovative Medicines Enterprise Business Review, Dec 5th, 2023 and IQVIA claims YTD extrapolated for FY 2023 and projected to 2036; 3. Approved IL-17 mAbs: COSENTYX (secukinamab), TALTZ (ixekinumba); 4. Development candidate definition: Ready for IND-enabling studies.

Financial Highlights

Financial Resources Forecast Extends Through Q4 2027

CASH, CASH EQUIVALENTS & MARKETABLE SECURITIES

$322.7M

as of
September 30, 2023

CASH RUNWAY

Q4 2027

INCLUDES

- **$60M** in milestones received from JNJ in Q4 2023
- **$300M** upfront from Takeda collaboration in Jan ’24

Does NOT INCLUDE

- **$215** in POTENTIAL milestones from JNJ over 18-36 months

SHARES OUTSTANDING

~57.6M

as of
September 30, 2023

Protagonist Therapeutics

Protagonist Therapeutics

Thank you

Protagonist Therapeutics

65th American Society of Hematology Annual Meeting & Exposition

Accepted Abstracts

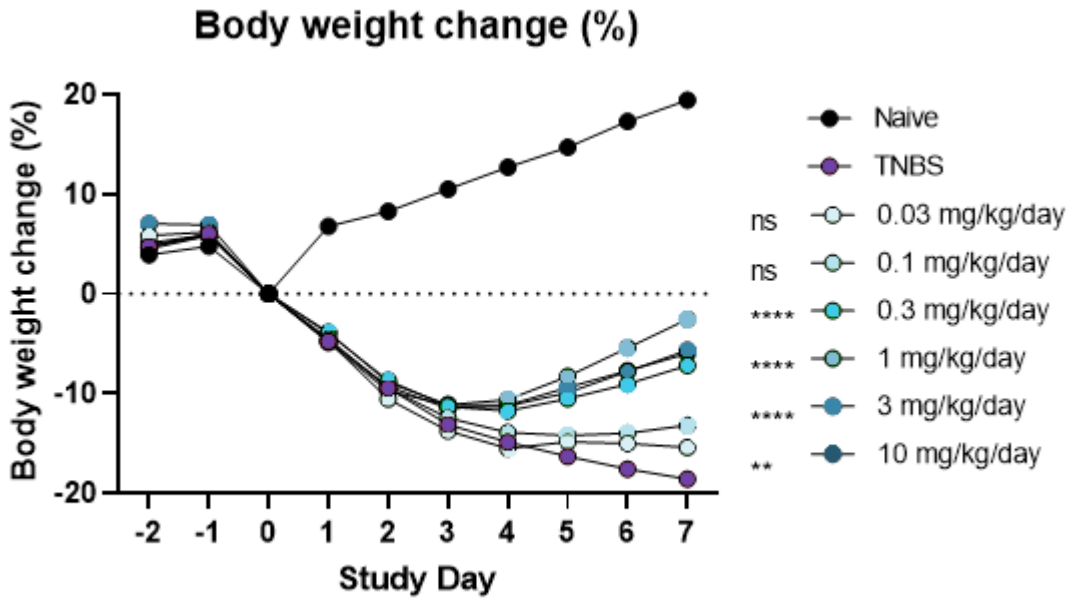
65th ASH Annual Meeting and Exposition (2023)

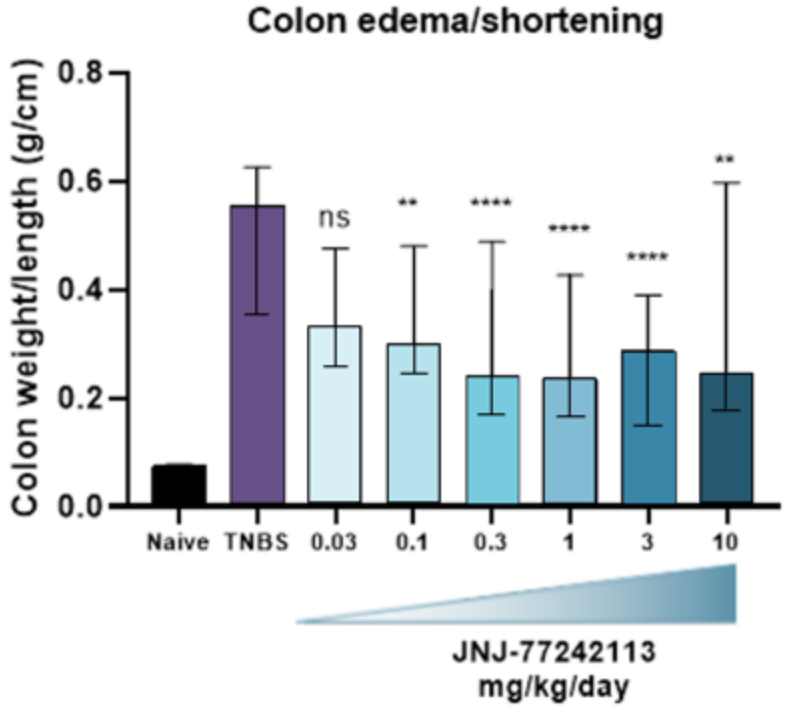
Company-Sponsored Abstracts

Day	Time (PST)	Type	Location	Presentation/Abstract Title	Abstract Number	Presenting Author	Abstract URL
Oral Presentations							
Sat 9 Dec	10:30 AM	Oral	Marriott Marquis San Diego Marina, Pacific Ballroom Salons 18-19	Real-World Analysis of Thromboembolic Event Rates in Patients in the United States with Polycythemia Vera	137	Kuykendall	https://ash.confex.com/ash/2023/webprogram/Paper180309.html
Mon 11 Dec	10:30 AM	Oral	San Diego Convention Center, Ballroom 20CD	Durability of Hematocrit Control in Polycythemia Vera with the First-in-Class Hepcidin Mimetic Rusfertide: Two-Year Follow up Results from the Revive Study	745	Ritchie	https://ash.confex.com/ash/2023/webprogram/Paper178253.html
Poster Presentations							
Sat 9 Dec	6:00 PM	Poster	San Diego Convention Center, Halls G-H	Prevalence of Second Cancers in Patients with Polycythemia Vera (PV): A Retrospective Analysis of US Real-World Claims Data	3190	Pemmaraju	https://ash.confex.com/ash/2023/webprogram/Paper180045.html
Sat 9 Dec	6:00 PM	Poster	San Diego Convention Center, Halls G-H	Iron Restricted Erythropoiesis Under Hepcidin Mimetic Treatment (PN23114) Improved Disease Parameters in a Mouse Model for Sickle Cell Disease	1117	Taranath	https://ash.confex.com/ash/2023/webprogram/Paper182472.html
Sun 10 Dec	6:00 PM	Poster	San Diego Convention Center, Halls G-H	Rusfertide Improves Markers of Iron Deficiency in Patients with Polycythemia Vera	3208	Ginzburg	https://ash.confex.com/ash/2023/webprogram/Paper178334.html

Pre-Clinical PoC 1: Rat TNBS-Induced Colitis Model

Orally Dosed JNJ-2113 Attenuates Weight Loss and Colon Inflammation





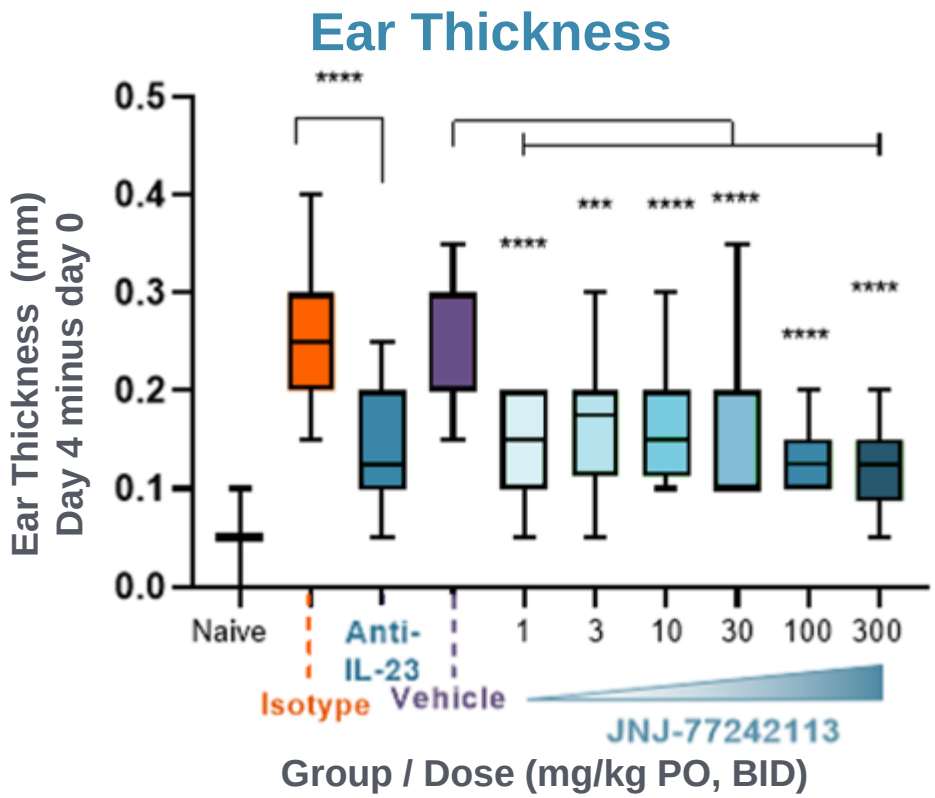
- **Statistically significant effects seen beginning at doses of 0.1 to 0.3 mg/kg/day**
- **Although exposure in plasma and skin was much lower than GI tissues, exquisite potency of JNJ-2113 indicated potential for systemic activity beyond the GI tract**

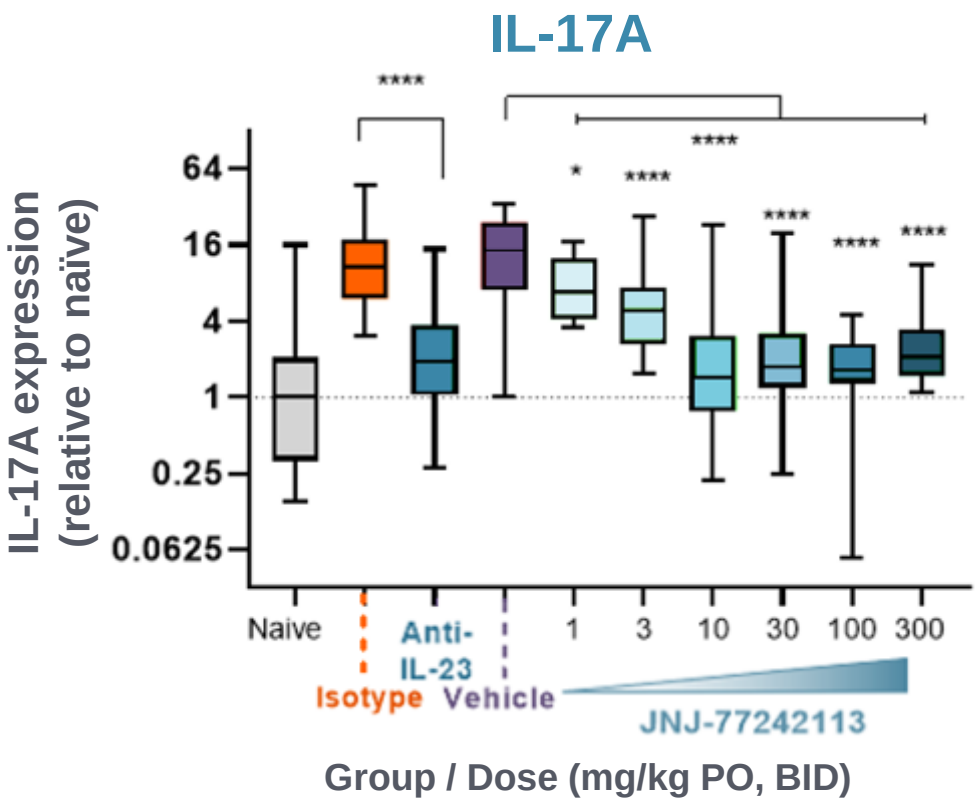
GI=Gastrointestinal; TNBS=Trinitrobenzenesulfonic acid.
ns=not significant, **p <0.01, ****p <0.0001. Graph on right represents median and interquartile range. Data combined from three studies.

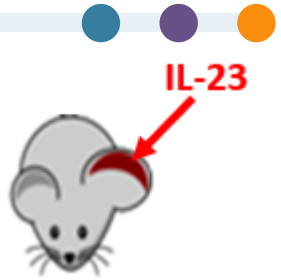
Fourie A, et al. ISID Meeting; May 10-13, 2023; Tokyo, Japan.

Pre-Clinical PoC 2: Rat IL-23 Induced Skin Inflammation Model

Orally Dosed JNJ-2113 Achieves Inhibition Equivalent to Anti-IL-23 Antibody







- **Doses ≥ 1 mg/kg BID reduced inflammation and cytokine induction (IL-17A, IL-17F and IL-22)**
- **Doses ≥ 10 mg/kg BID showed equivalent inhibition to an anti-IL-23 antibody**

BID=Twice daily. Anti-IL-23 and isotype control dosed intraperitoneally on days -1 and 3.
ns=not significant, *p <0.05, ***p <0.001, ****p <0.0001. Boxes depict median and interquartile ranges; bars depict minima and maxima. Data combined from three experiments.

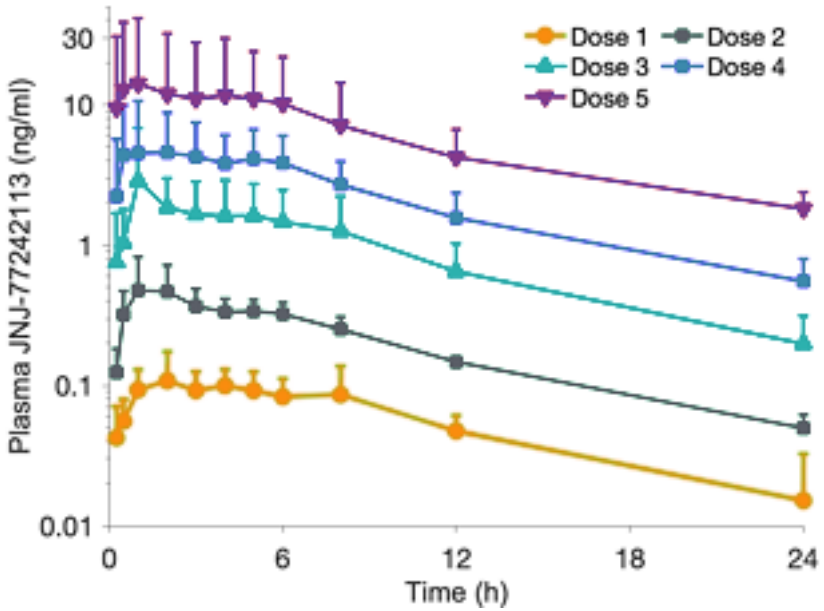
Fourie A, et al. ISID Meeting; May 10-13, 2023; Tokyo, Japan.

Protagonist Therapeutics

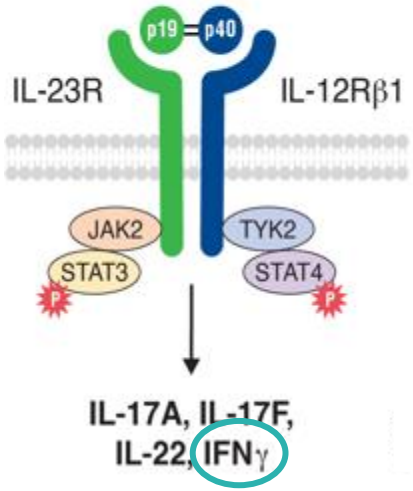
Phase 1 Study of JNJ-2113 in Healthy Volunteers

Safety, Pharmacokinetics, Systemic Pharmacodynamics

Human PK Profile† Supports Pathway Coverage

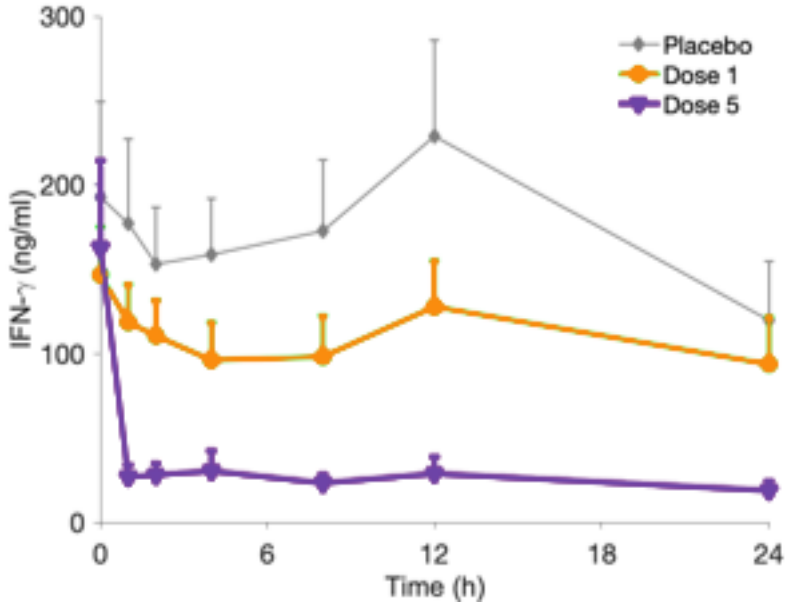


IL-23



Systemic PD: *ex vivo* IL-23-induced IFNγ in blood

Robust Systemic PD Activity with Oral Dosing



- **Demonstrated PoC for systemic PD activity of orally dosed JNJ-2113 in humans**
- **Single and multiple oral doses were safe and generally well tolerated with no safety signal of concern**

PD=Pharmacodynamic; PK=Pharmacokinetic; PoC=Proof of Concept.
PK data represent mean + SD.
†Phase 1 conducted under fasted conditions.

Protagonist Therapeutics

Fourie A, et al. ISID Meeting; May 10-13, 2023; Tokyo, Japan.

ICONIC-LEAD: JNJ-2113 Phase 3 Study in Moderate to Severe Plaque Psoriasis

A Study of JNJ-77242113 in Adolescent and Adult Participants with Moderate to Severe Plaque Psoriasis

n=600 (2:1 randomization)

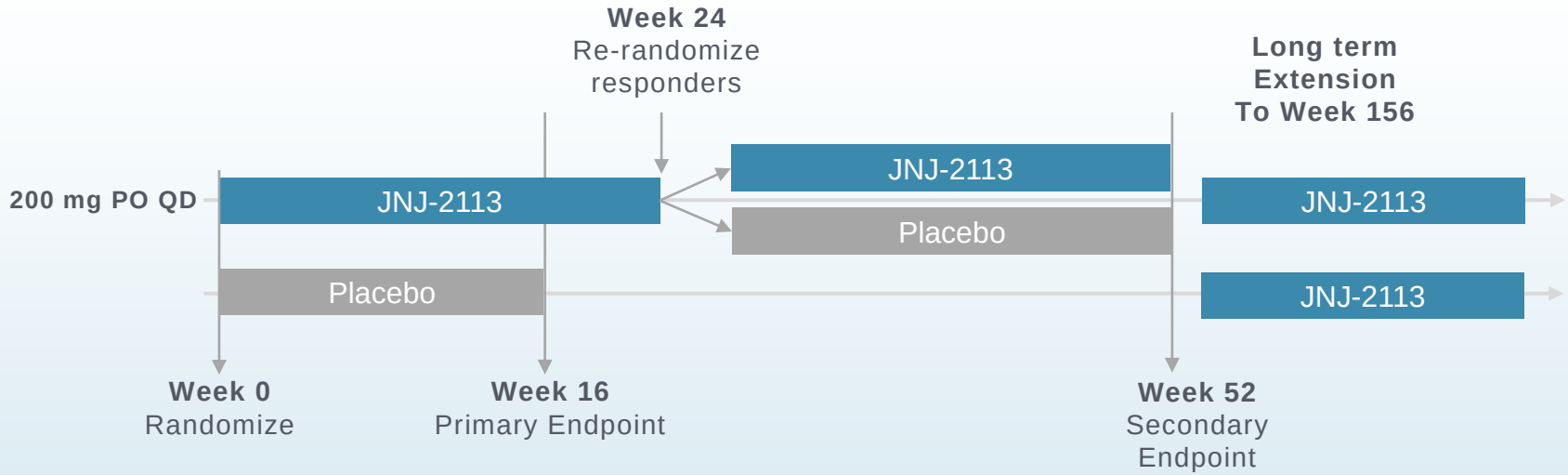
Eligibility:

Mod/Severe PsO
- IGA≥3
- PASI≥12
- BSA≥10%
- Age: ≥ 12

Primary endpoint:
- IGA 0/1 Week 16
- PASI 90 Week 16

Study Start Date: 10/12/23

Estimated Primary Completion:11/19/24



Protagonist Therapeutics

ICONIC-TOTAL: JNJ-2113 Phase 3 Study in Plaque Psoriasis Involving Special Areas

A Study of JNJ-77242113 for the treatment of Participants with Plaque Psoriasis Involving Special Areas (Scalp, Genital, and/or Palms of the Hands and the Soles of the Feet)

n=300 (2:1 randomization)

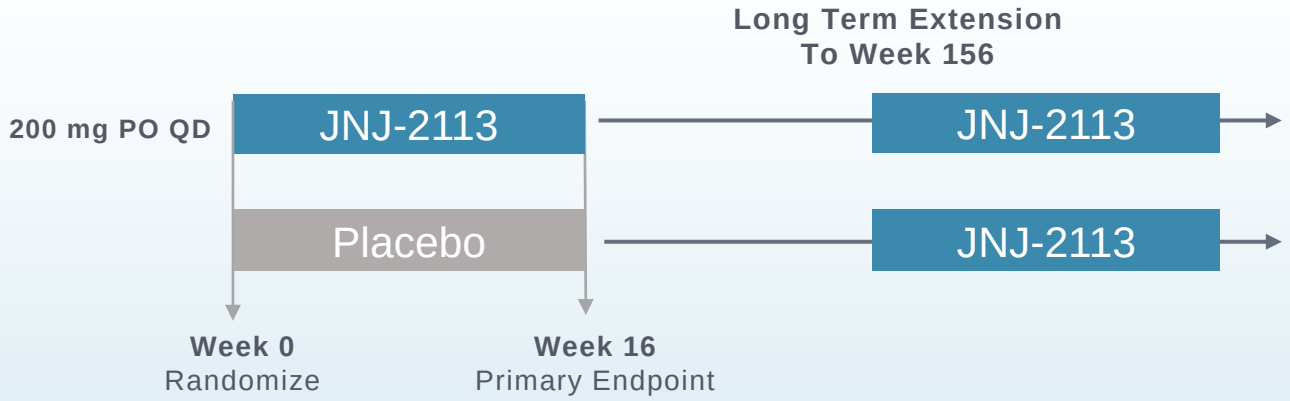
Eligibility:

Special Areas and Low BSA Mod-Severe
•IGA≥2 + BSA ≥ 1% + mod/severe special area (ss-IGA≥3 or sPGA of genitalia≥ 3 or hf-IGA≥3) OR
•IGA≥3, BSA 5-10%
•Failed Topicals
• Age: ≥ 12

Primary endpoint:
- IGA 0/1 Week 16

Study Start Date: 10/12/23

Estimated Primary Completion: 11/5/24



Protagonist Therapeutics

ICONIC-Advance 1: JNJ-2113 Phase 3 Study in Moderate to Severe Plaque Psoriasis (Head-to-Head Versus Deucravacitinib)

A Study of JNJ-77242113 in Adolescent and Adult Participants with Moderate to Severe Plaque Psoriasis

2:1:2 randomization
2113/placebo/deucra, n=750*

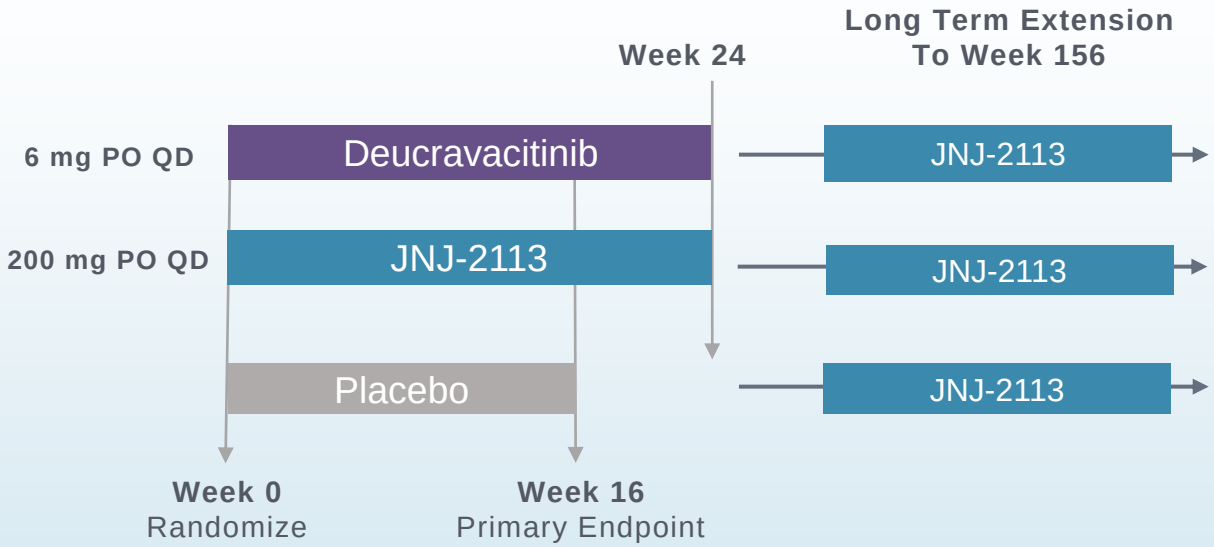
Eligibility:

Mod/Severe PsO
- IGA≥3
- PASI≥12
- BSA≥10%
- Age: ≥ 18

Primary endpoint:
- IGA 0/1 Week 16
- PASI 90 Week 16

Estimated Study Start Date: 2/9/24

Estimated Primary Completion: 3/13/25



*Study powered for JNJ-2113 superiority to placebo and deucravacitinib

Protagonist Therapeutics

ICONIC-Advance 2: Second JNJ-2113 Phase 3 Study in Moderate to Severe Plaque Psoriasis (Head-to-Head Versus Deucravacitinib)

A Study of JNJ-77242113 in Adolescent and Adult Participants with Moderate to Severe Plaque Psoriasis

4:1:4 randomization
2113/placebo/deucra, n=675*

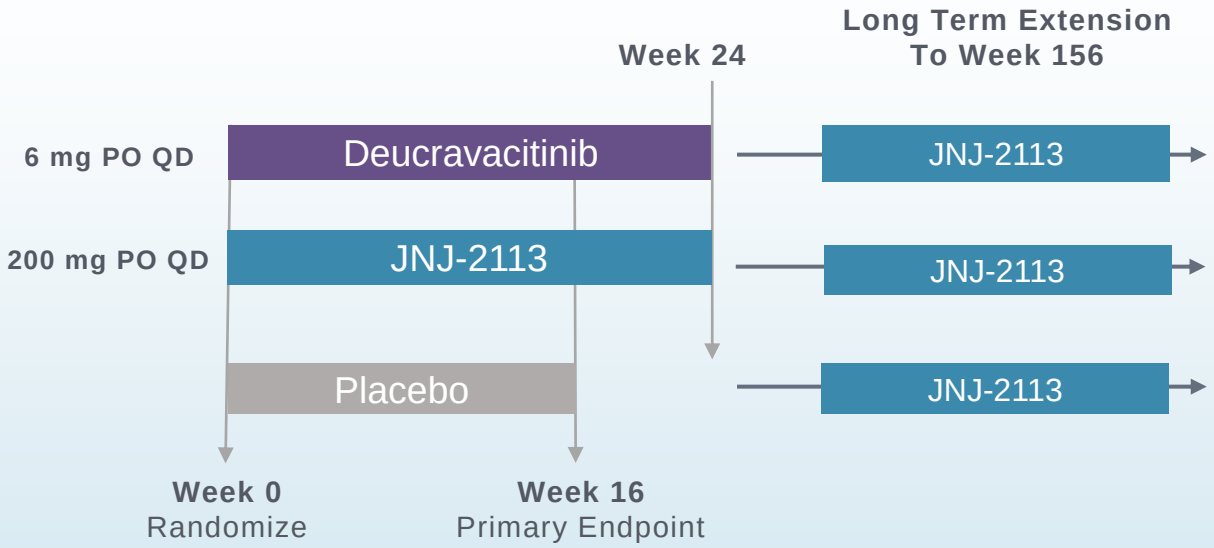
Eligibility:

Mod/Severe PsO
- IGA≥3
- PASI≥12
- BSA≥10%
- Age: ≥ 18

Primary endpoint:
- IGA 0/1 Week 16
- PASI 90 Week 16

Estimated Study Start Date: N/A

Estimated Primary Completion: N/A



*Study powered for JNJ-2113 superiority to placebo and deucravacitinib

Protagonist Therapeutics

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

A Study of JNJ-77242113 in Participants With Moderately to Severely Active Ulcerative Colitis (ANTHEM-UC)

Adult Patients with UC

n=~240

Eligibility:

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

Primary endpoint:

- Clinical Response (Modified Mayo score) at Week 12

Study Start: 10/9/23

Estimated Primary Completion: 5/27/25