Protagonist Therapeutics

COMPANY OVERVIEW

Dinesh V. Patel, PhD | President & CEO

November 2022

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 related to potential future collaboration arrangements, the impact on our business or product candidates of actions or determinations of the U.S. Food and Drug Administration ("FDA"), enrollment in our clinical trials, any potential impact on our business related to COVID-19, our potential receipt of milestone payments and royalties under our Collaboration Agreement with Janssen Biotech, Inc., 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.

This presentation concerns products that are under clinical investigation and which have not yet been approved for marketing by the U.S. Food and Drug Administration. They are currently limited by Federal law to investigational use, and no representation is made as to their safety or effectiveness for the purposes for which they are being investigated. The trademarks included herein are the property of the owners thereof and are used for reference purposes only. Such use should not be construed as an endorsement of such products. Nothing contained in this presentation is, or should be construed as, a recommendation, promise or representation by the presenter or Protagonist or any director, employee, agent or advisor of Protagonist. This presentation does not purport to be all inclusive or to contain all the information you may desire.

Protagonist Therapeutics

Ongoing Ph3 Study of Rusfertide in PV | Collaboration with Janssen Toward Oral IL-23R Antagonist

- **Robust, advancing peptide therapeutic candidate portfolio** addressing indications with multi-billion-dollar market potential

  Rusfertide, an investigational, injectable hepcidin mimetic

  - Ongoing execution of VERIFY, the Phase 3, global, randomized, placebo-controlled trial evaluating the efficacy and safety of a once weekly, subcutaneously self-administered dose of rusfertide in polycythemia vera (PV)

- **Co-Development partnership portfolio earned $112.5 Million in milestone payments to date; potential up to $855 Million future milestones**
  - Granted **Janssen Biotech** an exclusive worldwide license to research, develop and commercialize oral IL-23 receptor antagonists
  - **PN-235**
    - ❖ FRONTIER 1, FRONTIER 2, and SUMMIT Phase 2 studies initiated in moderate-to-severe psoriasis
    - ❖ Phase 1 Asian NHV population studies

Strong cash position, with cash runway through the end of 2024

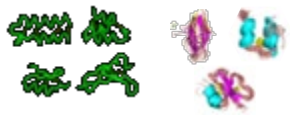
Protagonist Therapeutics

Peptide-based Medicines

Discovering novel peptide therapeutics through a proprietary technology platform and developing them to address unmet medical needs

POTENCY

1 **Computational**
Vectrix, Clusters



Vectrix® Clusters

2 **Phage Libraries**
Hits

3 **Peptide Chemistry**
SAR, Leads

STABILITY

4 **Oral Stability**
Peptidomimetics
GI Assays

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

6 **Systemic Availability**
Formulation
SAR, Transport

CLINICAL ASSETS IN LATE-STAGE DEVELOPMENT

Rusfertide (Ph3)

PN-235 (Ph2)

Product Portfolio

Addressing Unmet Needs in Multiple Indications with Multi-Billion Dollar Market Potential

Programs	Candidates	Study	Phase 1	Phase 2	Phase 3	Key Milestones
HEMATOLOGY & BLOOD DISORDERS						
		POLYCYTHEMIA VERA (PV)				
Hepcidin Mimetic	**Rusfertide (PTG-300)**	VERIFY	**PV Ph3 trial**			• ~250 patient, randomized, double-blind, placebo-controlled study • Enrollment completion expected by 2H 2023
		REVIEW	PV Ph2 PoC trial			• ~70 patient enrollment completed • Randomized portion completed by January 2023, continuing in OLE
		PACIFIC	PV Ph2 elevated HcT (>48%) trial			• 16 patients completed 16-week study, continuing in OLE
INFLAMMATORY & IMMUNOMODULATORY DISEASES						
Oral IL-23R Antagonist	**PN-235** JNJ-77242113	FRONTIER-1	**Psoriasis Ph2b PoC trial**		Janssen	• 240 patient FRONTIER-1 psoriasis study • FRONTIER 2 long-term extension study • 80 patient SUMMIT study with new formulation • Phase 1 NHV study • Psoriasis Ph3 decision expected in 2023 • IBD Ph2 Initiation expected in 2023
		SUMMIT	**Psoriasis Ph2b PoC trial**			

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Rusfertide (PTG-300): Hepcidin Mimetic

To Potentially Address Unmet Needs in Polycythemia Vera

Polycythemia Vera

Disease Background

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

- Elevated hematocrit (HCT) is a hallmark of the disease, indicating overproduction of RBCs

Serious, chronic disease associated with increased thrombotic and cardiovascular risks

Rare disease with ~100,000 diagnosed patients in US

- 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

Current treatments for PV are inadequate relative to need in HCT control and symptoms management

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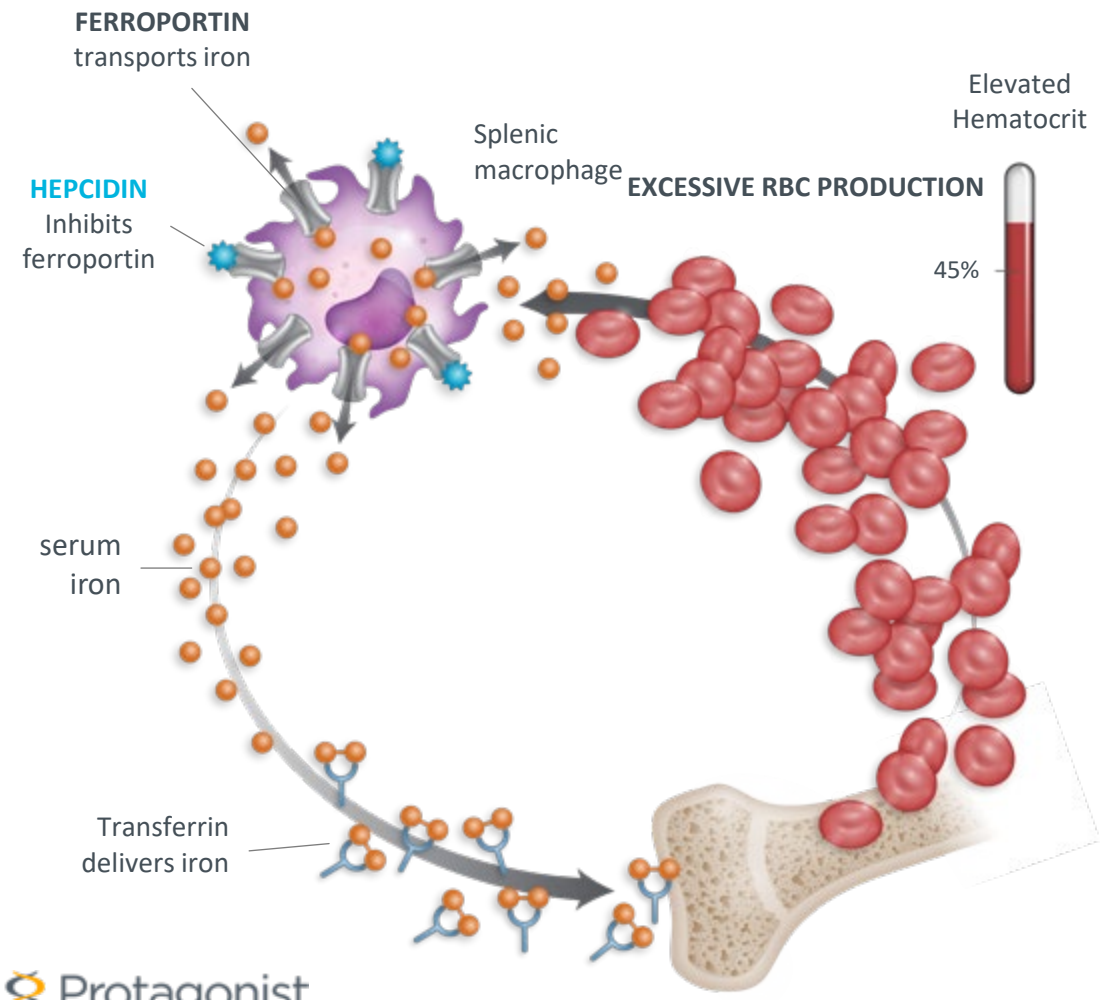
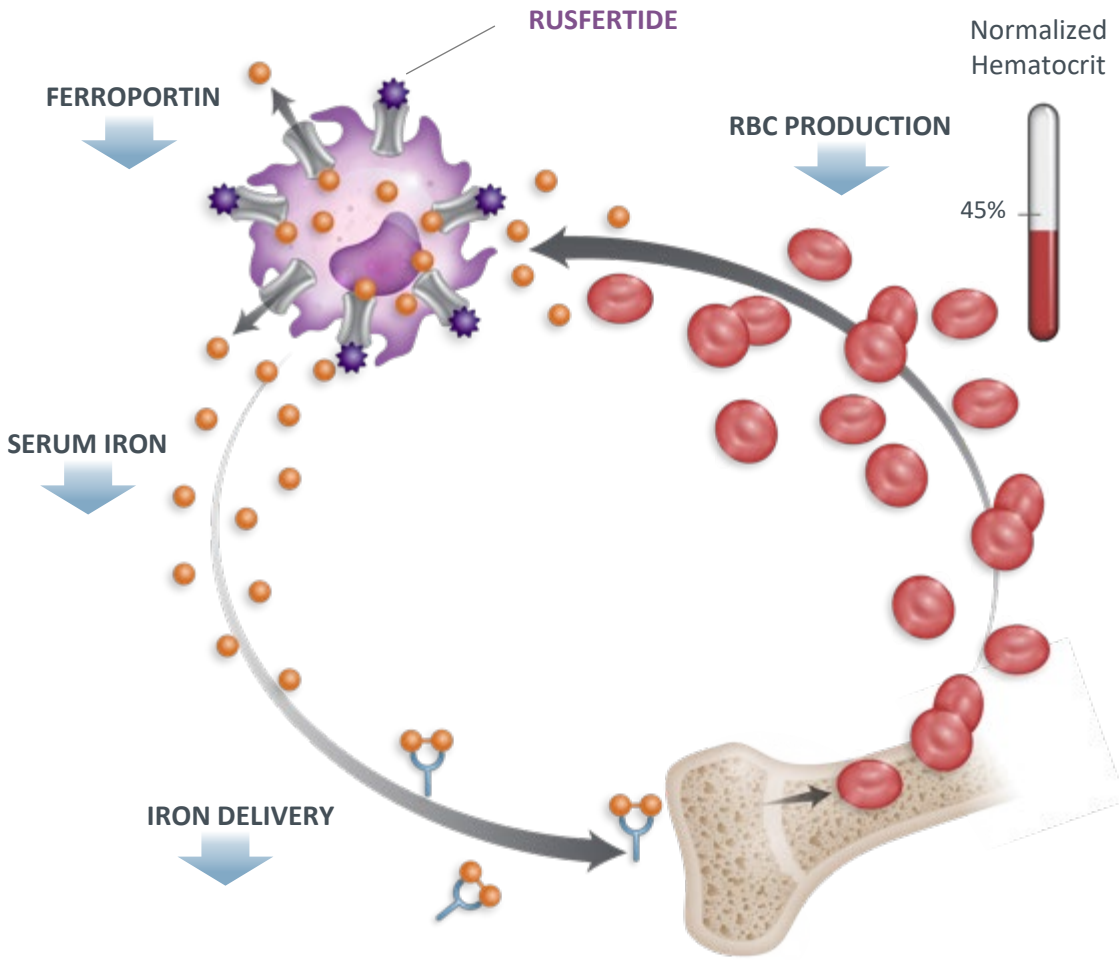
Rusfertide: Mechanistic Rationale for Potential Treatment of PV

Polycythemia Vera



MOA of rusfertide



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Rusfertide for Polycythemia Vera

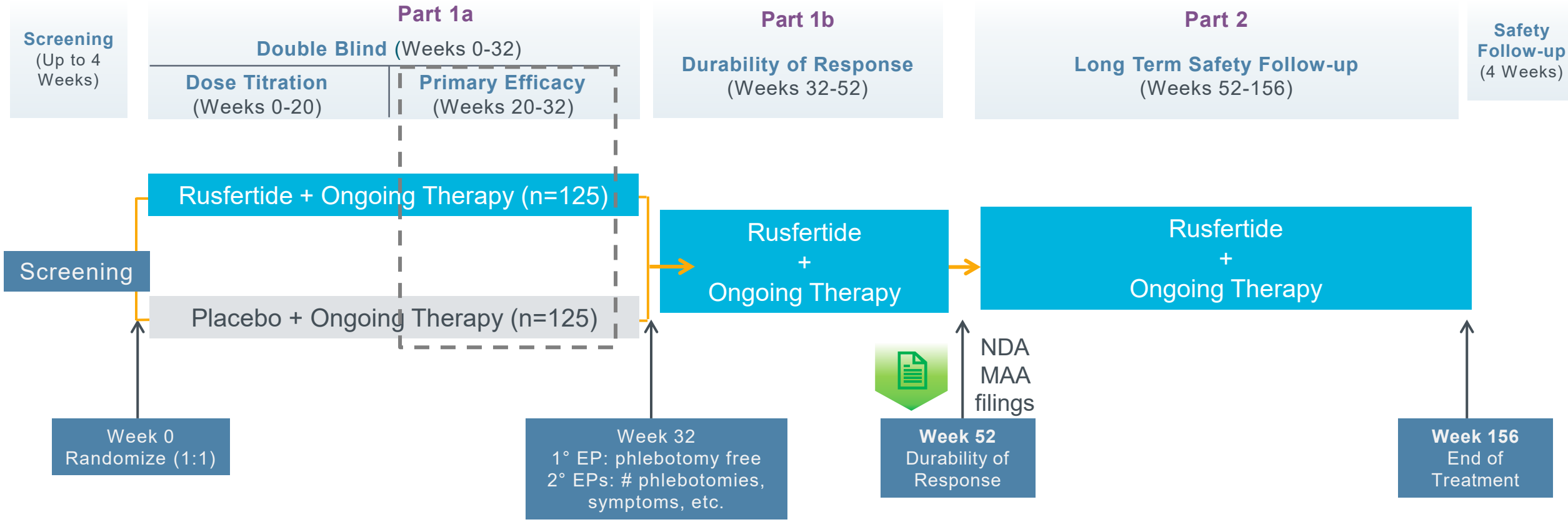
Three Clinical Studies Have Generated Positive Data

Ph3 VERIFY, Ph2 REVIVE, Ph2 PACIFIC

- Phase 3 **VERIFY** Study:
  - Study execution continues with enrollment completion expected in 2H 2023
  - Agreed upon Phase 3 VERIFY protocol with the FDA and CHMP (EU)
  - Agreements in place for US NDA
    - Non-clinical studies including two-year rat carcinogenicity study
    - Non-clinical and clinical pharmacology studies
    - Chemistry, Manufacturing and Controls plan
- Phase 2 **REVIVE** Study:
  - Clinical updates presented at ASH 2021, ASCO 2022, and EHA 2022; poster presentations at ASH 2022
    - Most recent Phase 2 data, presented at ASCO 2022, demonstrates the effects of dosing interruption and resumption
  - Enrollment complete; post-hold re-enrollment rate of >85%
- Phase 2 **PACIFIC** Study:
  - High hematocrit (HCT >48%) 16-week study completed; subjects in OLE
- Rusfertide has received Orphan Drug designation and Fast Track status

Randomized, Double-blind, Placebo-Controlled Phase 3 PV Study (VERIFY)

Ongoing VERIFY Study of N~250 Subjects



The Phase 3 study design capitalizes on the successful outcome to date of the 60-plus patient open-label Phase 2 REVIVE Study

In consultation with the U.S. Food and Drug Administration, Protagonist has implemented a set of safety monitoring procedures in all ongoing clinical studies, including cancer surveillance measures (dermatological examinations) and stopping rules.

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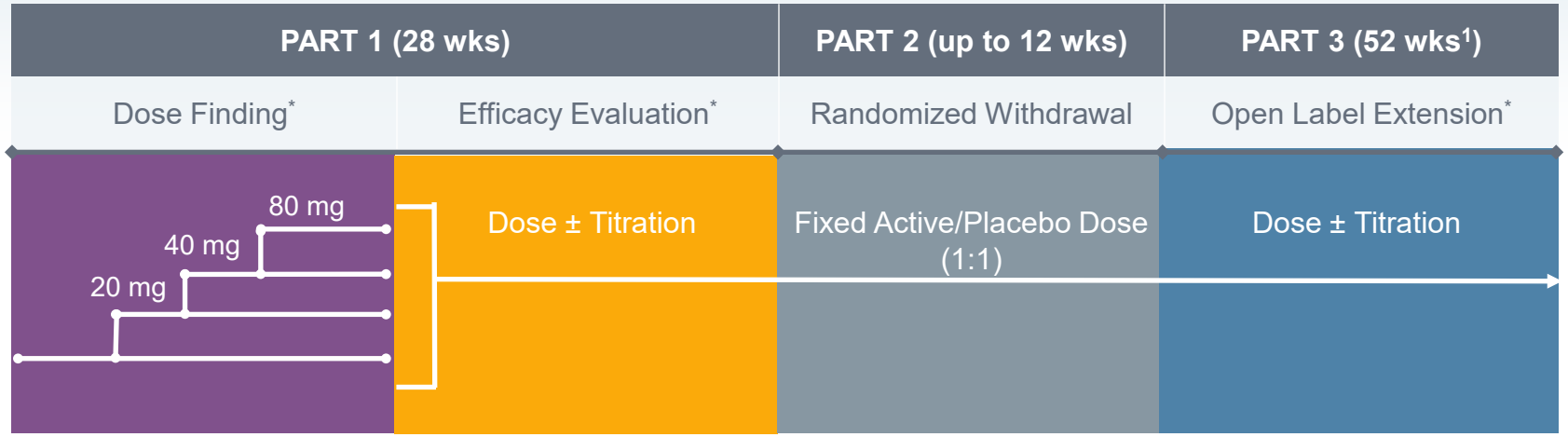
Phase 2 Study of Rusfertide in PV Patients (REVIVE)

GOAL: Maintain Hematocrit <45%

Clinical Proof-of-Concept Study with Add-On



- **Titrate every 4 weeks to maintain hematocrit < 45%*
- *[1]OLE increased from 52 weeks to 3 years*

ELIGIBILITY REQUIREMENTS:

- Phlebotomy dependent PV patients diagnosed as per 2016 WHO criteria
- ≥3 phlebotomies in 6 months with or without concurrent cytoreductive therapy
- Rusfertide (PTG-300) doses of 10-80 mg administered subcutaneously weekly added to prior standard therapy

KEY ENDPOINTS:

Safety
Maintain Hematocrit <45%
Reduction in Phlebotomies
Symptom Scores: MPN-SAF TSS, PGI-C

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Baseline Characteristics of Study Participants in REVIVE Study

Characteristics (n = 70)

AGE	
Range	27-77 years (Mean = 57.3 yrs)
GENDER	
Females	21 (30.0%)
Males	49 (70.0%)
RISK	
Low	29 (41.4%)
High	41 (58.6%) [Age based – 37.1%, Thrombotic events – 21.4%]
DURATION SINCE PV DIAGNOSIS	
<1 yr	14 (20.0%)
1 - <3 yrs	24 (34.3%)
3 - <5 yrs	11 (15.7%)
≥5 yrs	21 (30.0%)

THERAPIES	
PHL only	34 (48.6%)
PHL + HU	21 (30.0%)
PHL + IFN	8 (11.4%)
PHL + RUX	3 (4.3%)
PHL +Multiple Agents	4 (5.7%)
NUMBER OF PHL IN 28 WEEKS PRIOR	
2-3	14 (20.0%)
4-5	38 (54.3%)
≥6	18 (25.7%)
Median	4.79
DAYS BETWEEN PHLEBOTOMIES	
Median	34

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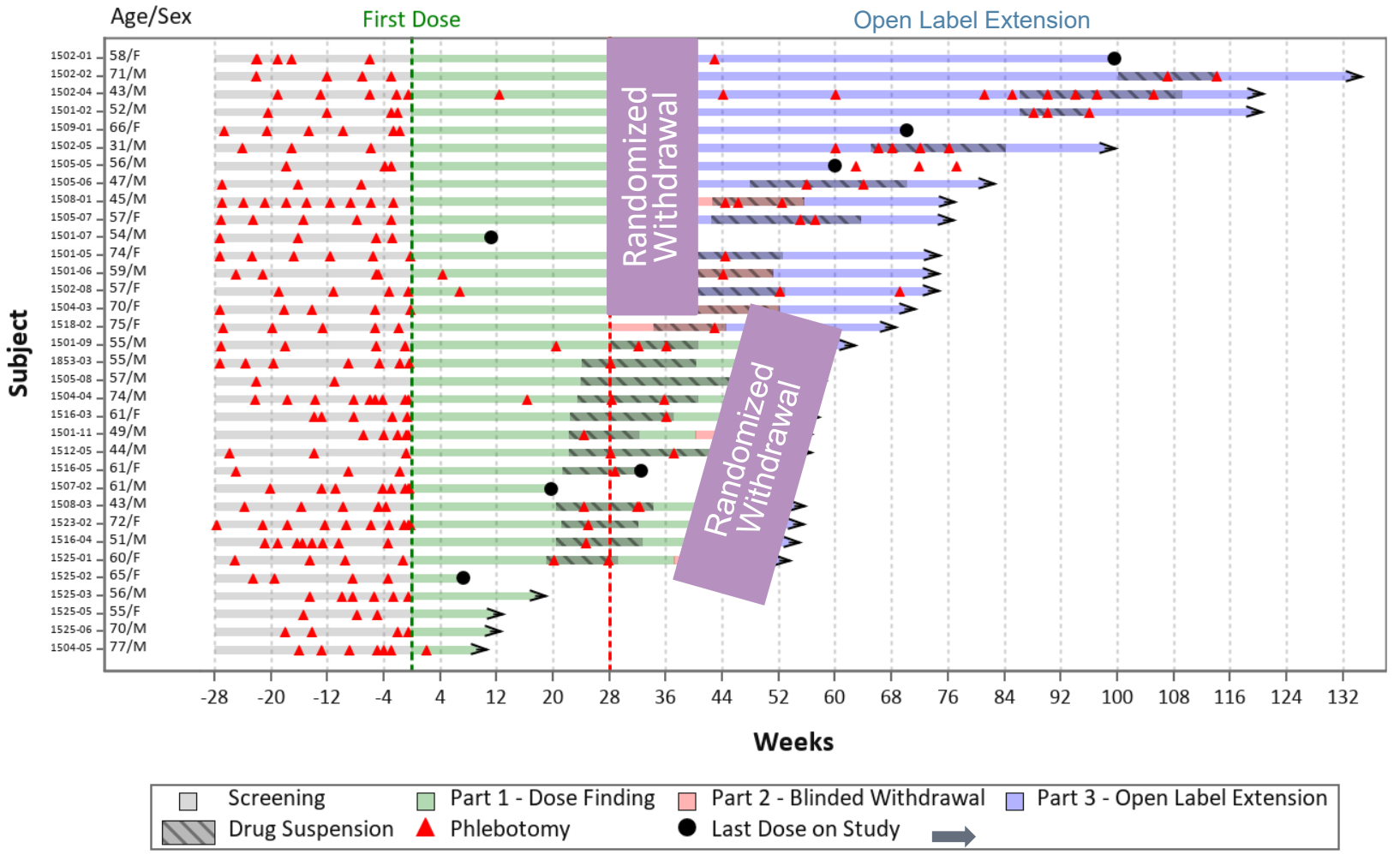
Enrollment complete. Data as of March 10, 2022, and as presented at ASCO June 2022

Meaningful Reduction in Phlebotomy Frequency Following Rusfertide Administration

Phlebotomy Only (n=34)



Data cutoff: May 11, 2022

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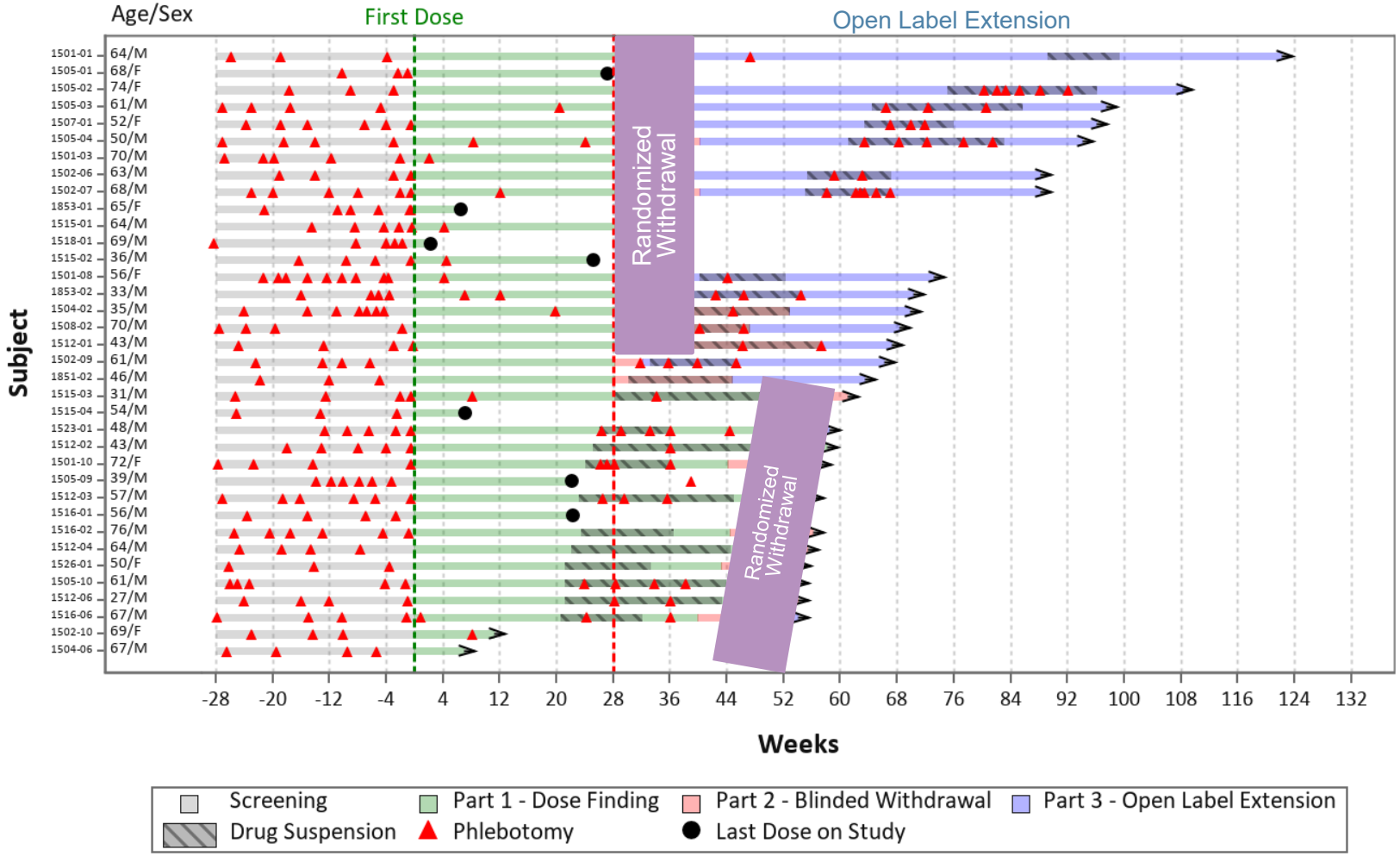
Meaningful Reduction in Phlebotomy Frequency Following Rusfertide Administration

Phlebotomy and Cytoreductives (n=36)



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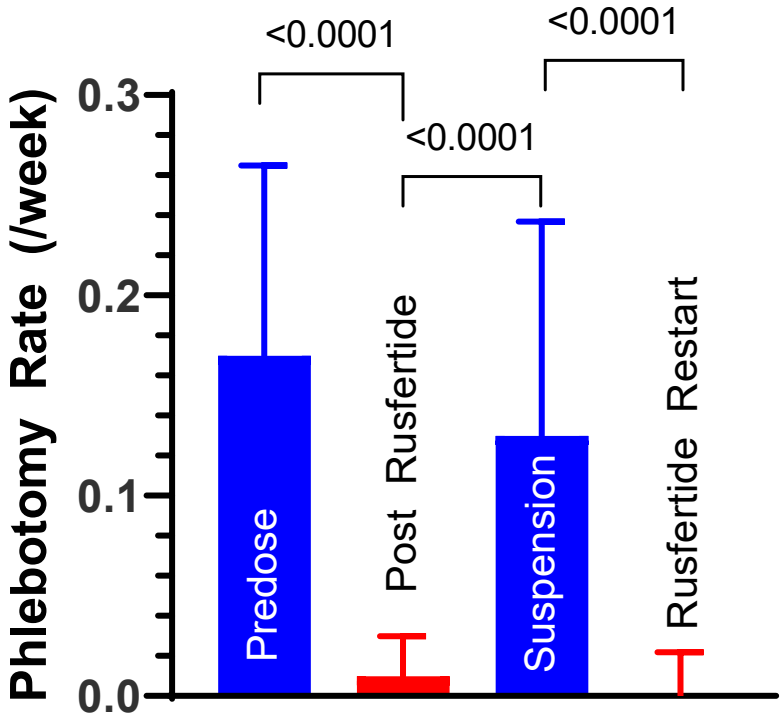
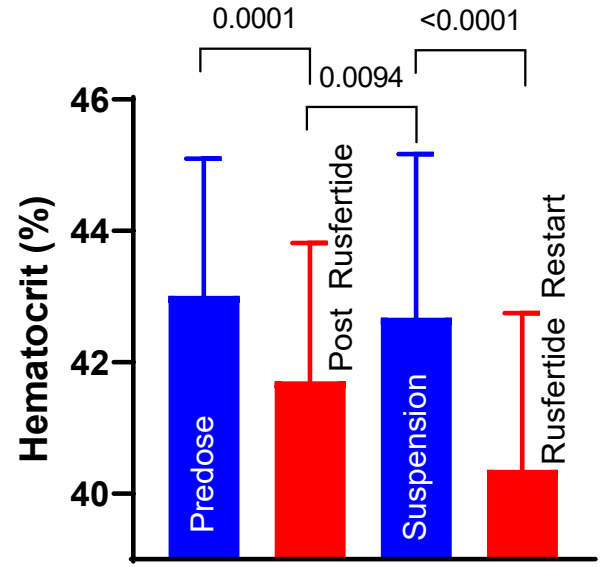
REVIVE Study: Rusfertide Treatment Suspension Led to Loss of Effect

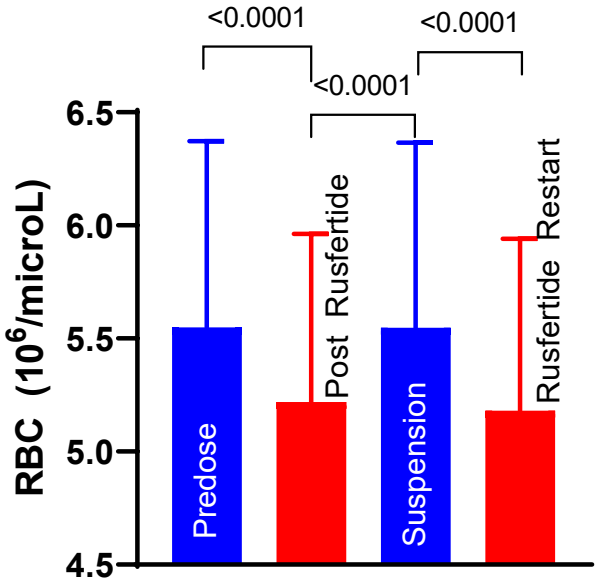
Data Provides Additional Evidence Supporting Clinical Efficacy

Treatment Restart Restores Benefit



During the brief clinical hold patients were maintained on their cytoreductive regimens and had TP for HCT >45%. The clinical protocol was amended to add this information, dermatological screening, and stopping rules and rusfertide was reinitiated following patient reconsent. Most patients (85%) returned to Rusfertide add-on treatment 2-3 months after the dosing interruption and reinitiation





n=48*

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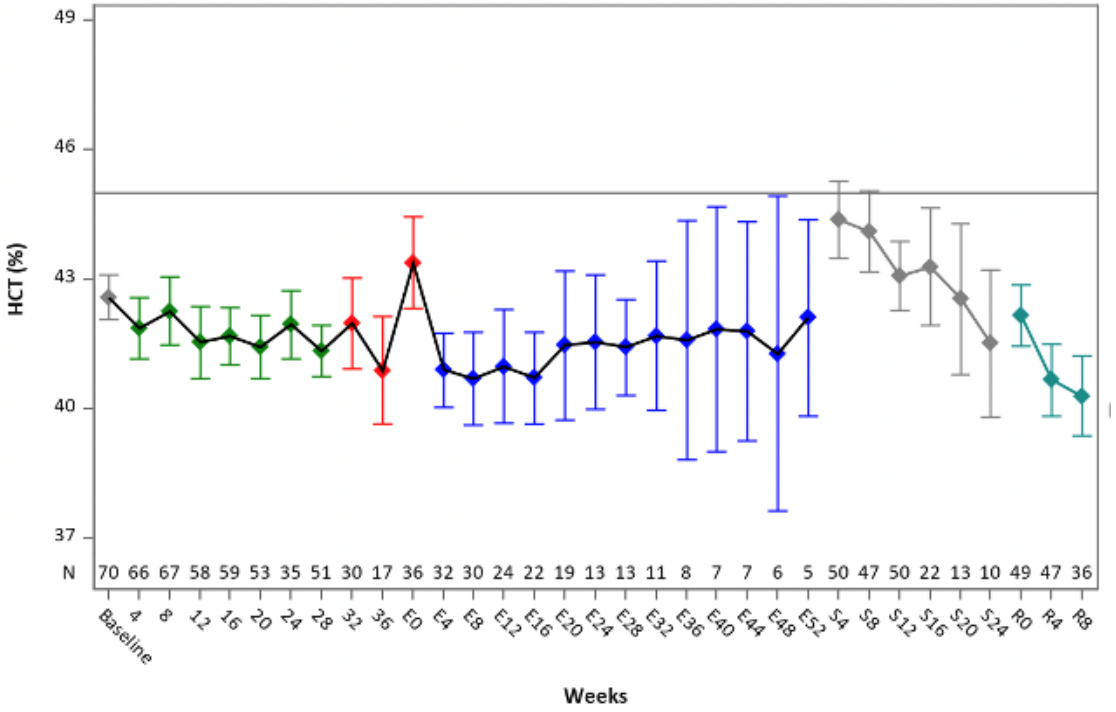
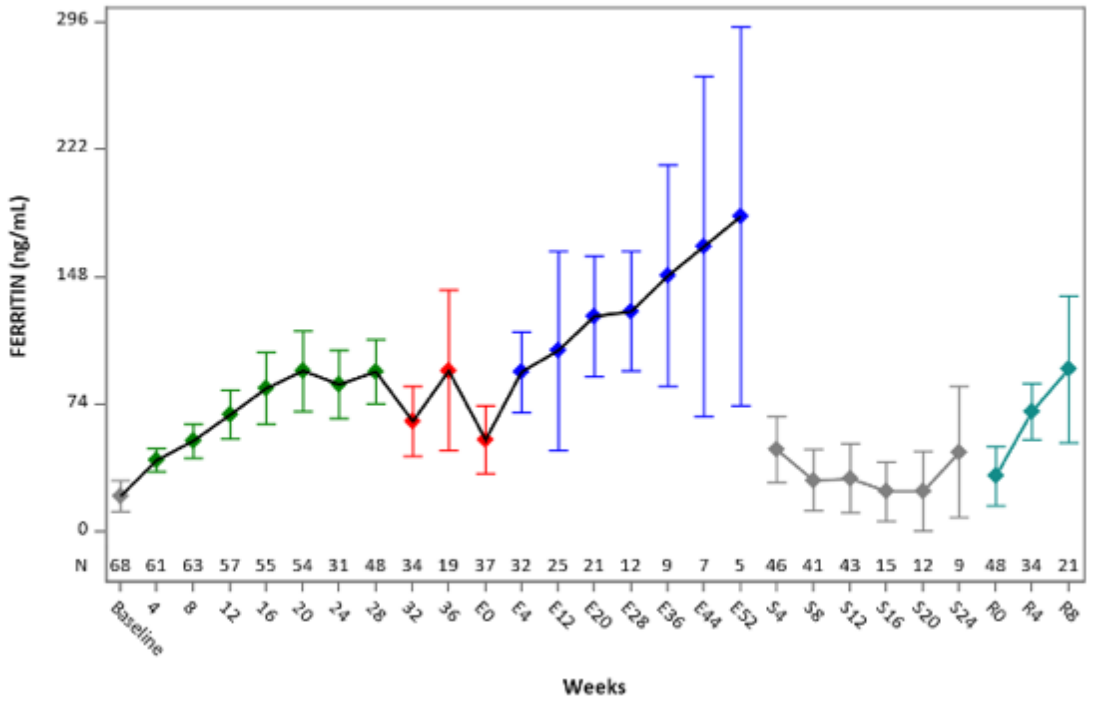
Data cutoff: May 11, 2022
*Subjects with complete restart data

Rusfertide Controlled HCT and Ferritin in REVIVE Study

Hematocrit



Ferritin



Screening | Part 1 – Dose Finding | Part 2/3 – Blinded Withdrawal/OLE | Part 3 – Open Label Extension

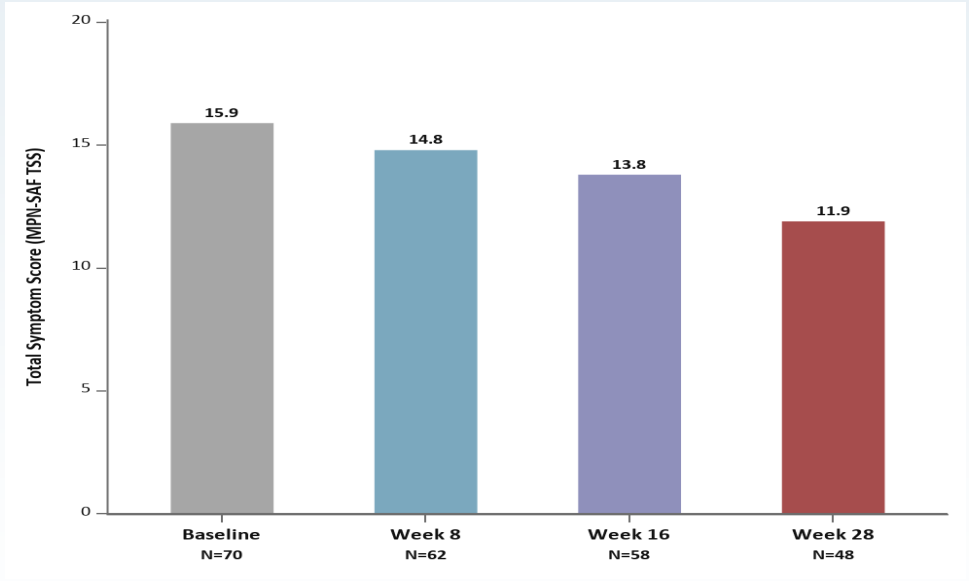
Error bars identify 95% confidence interval for the mean.

Data as of May 11, 2022

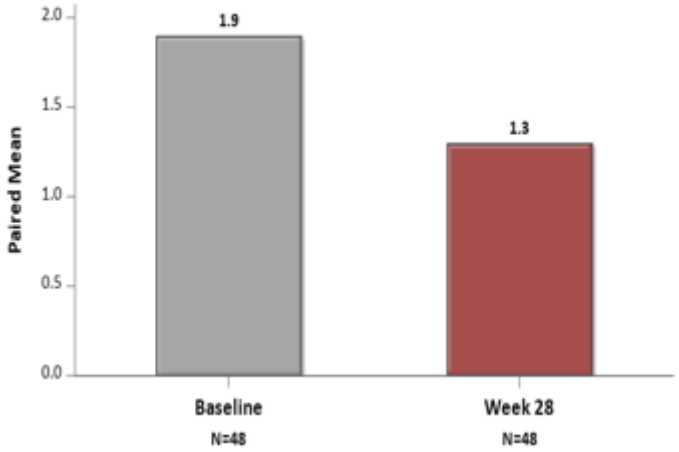
Improvement in Symptom Scores Following Rusfertide in REVIVE Study

Myeloproliferative Neoplasm Symptom Assessment Form Total Symptom Score (MPN-TSS)

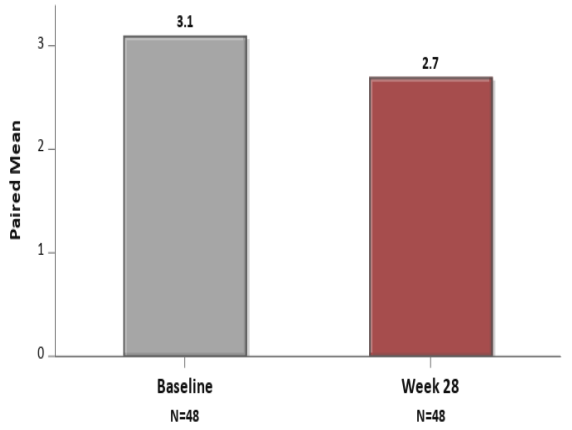
Total Symptom Score



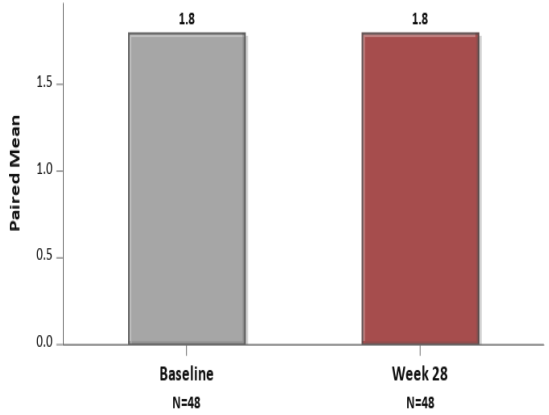
Problems with Concentration



Worst Level of Fatigue



Itching-Pruritus



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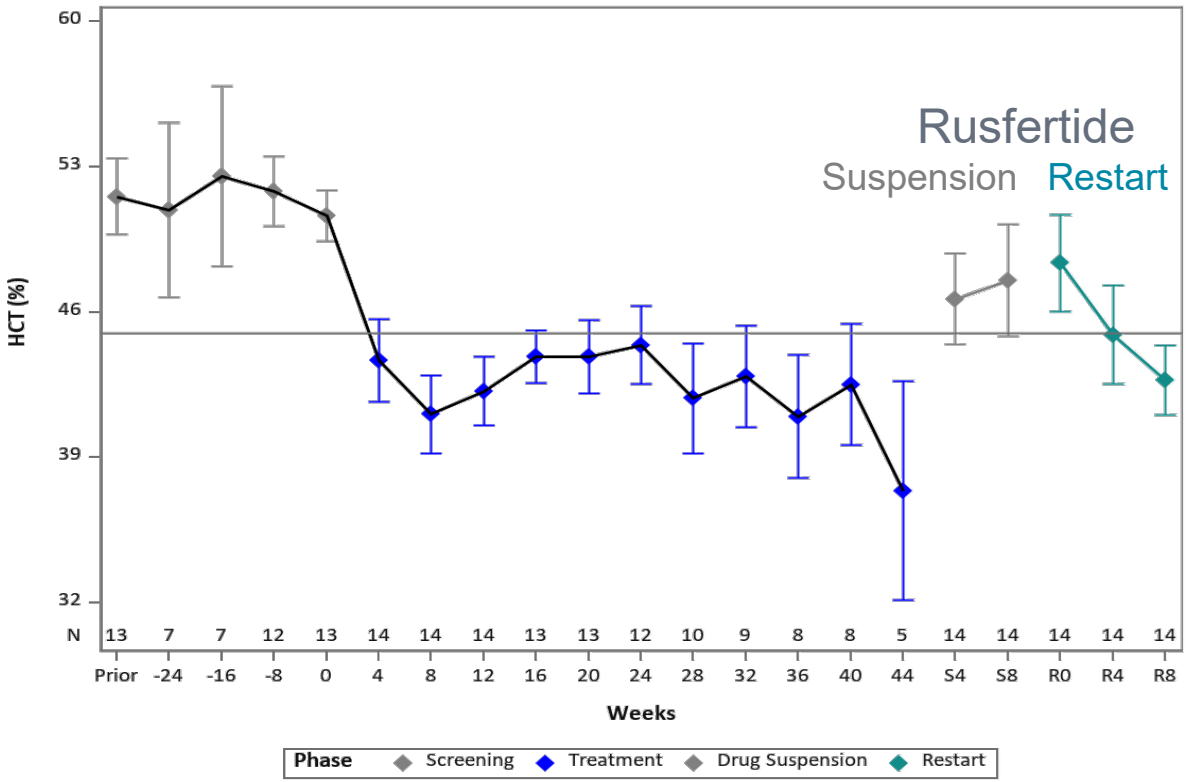
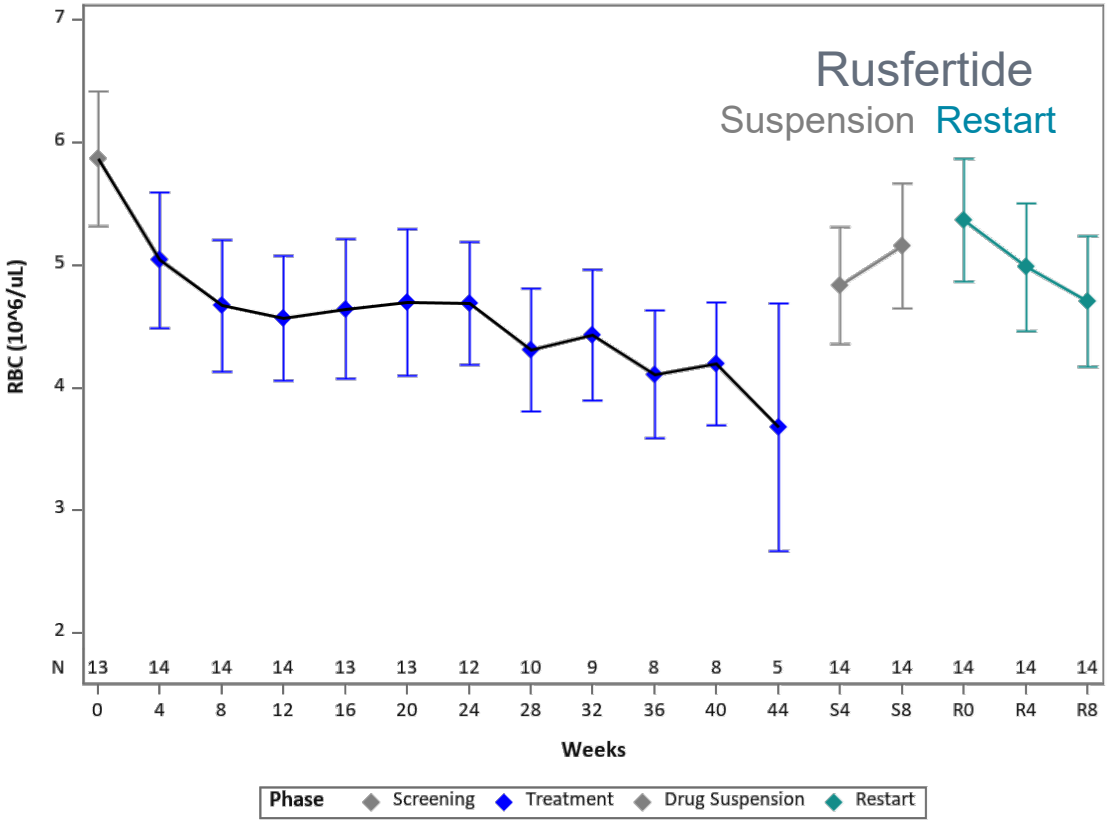
Data as of May 11, 2022

Rusfertide Lowered Hematocrit Levels Before and After Drug Suspension Period

PACIFIC Study in PV Patients with High HCT (>48%), n=14*





Error bars identify 95% confidence interval for the mean.
Data cutoff: May 11, 2022,
*Subjects with complete restart data

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Adverse Events Following Rusfertide in Patients with PV

REVIVE and PACIFIC Studies

Most treatment related AEs were Grade 1 or 2

- Injection site reaction (ISRs) were most common and associated with 33% of injections. All ISRs were transient, and no patient discontinued due to an ISR
- **SAE**'s include aneurysm of popliteal artery, atrial fibrillation, chest pain, hydrocephalus, gastroenteritis, syncope, basal cell carcinoma, squamous cell carcinoma, melanoma, AML, bowel obstruction, non-STEMI, hemoptysis
- No grade 3 events related to rusfertide
- One grade 4 event possibly related to rusfertide (asymptomatic thrombocytosis of about 1.2 million). Two withdrawals due to possibly related AE - both asymptomatic thrombocytosis.
- No clinically significant laboratory abnormalities.
- No Anti Drug Antibody response was noted in any patient

Preferred term	AE n (%)
Total number of Subjects	***90***
Injection site reaction	74 (82.2%)
Fatigue	20 (22.2)
Headache	20 (22.2)
Pruritis	19 (21.1)
Arthralgia	17 (18.9)
Dizziness	17 (18.9)
Nausea	16 (17.8)
Anemia	13 (14.4)
COVID-19	12 (13.3)
Diarrhea	11 (12.2)
Myalgia	10 (11.1)
Dyspnea	9 (10.0)
Hyperhidrosis	9 (10.0)

Treatment-emergent AEs with 10% or more incidence

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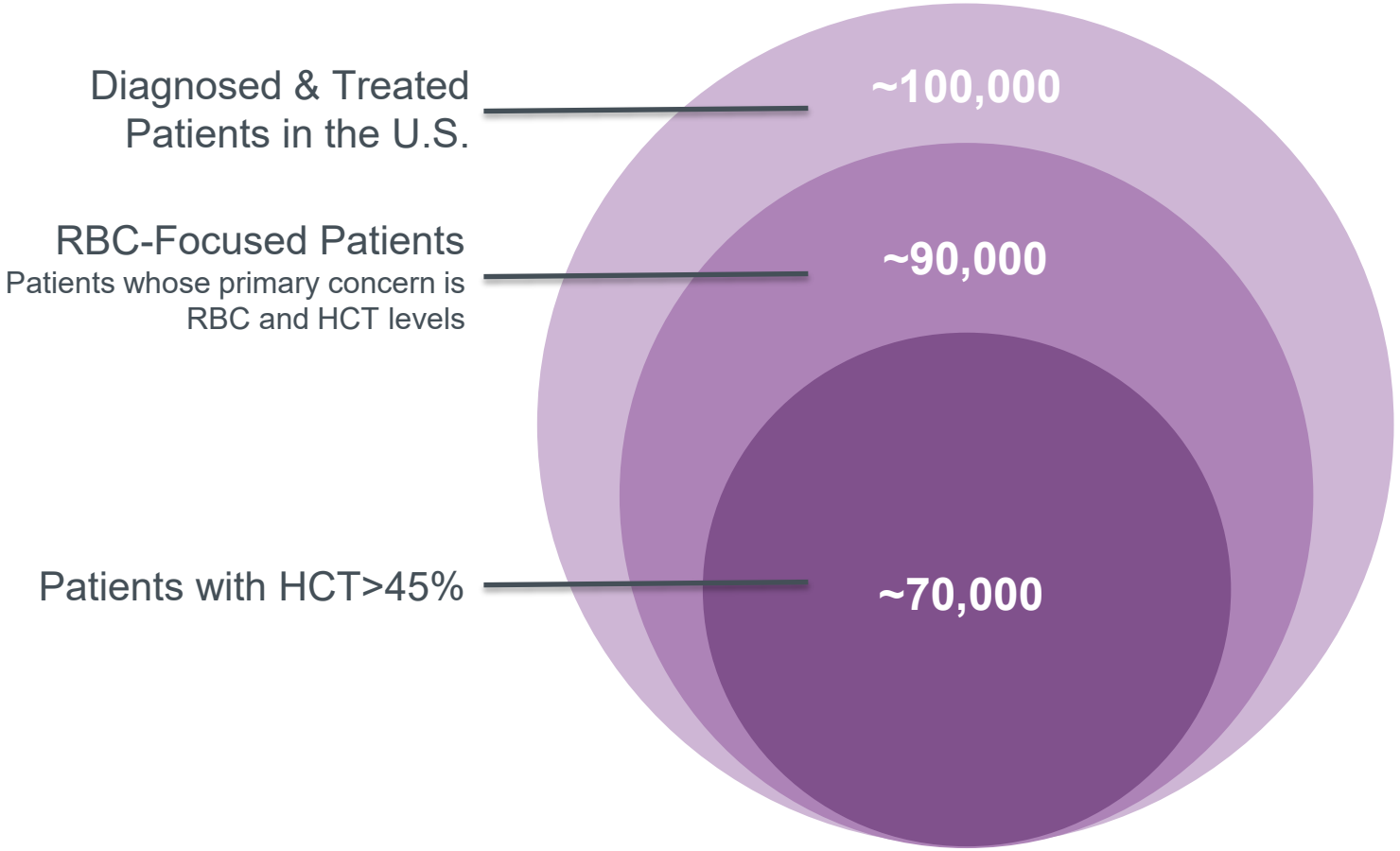
Data cutoff: June 23, 2022

Potential Commercial Opportunity

PV Patients Primarily Requiring HCT Control



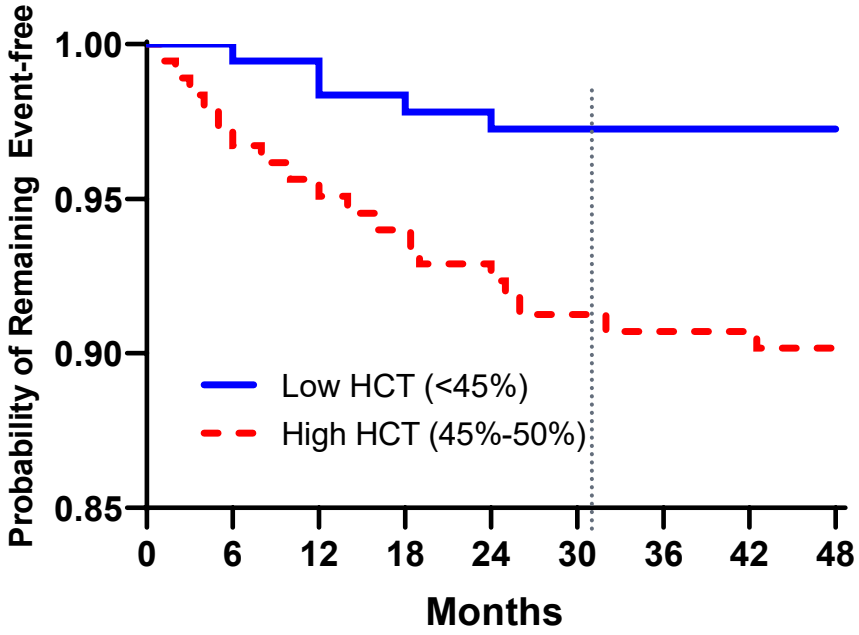
Based on internal metrics and third-party research

Elevated Hematocrit Results in Greater Risk of Death

Death from CV or Major Thrombotic Events Endpoint

- Patients randomized to <45% (Low) or 45 – 50% (High) HCT group
- At a median of 31 months, 9.8% of the High HCT group met the primary endpoint vs 2.7% in the Low HCT group

Patients with hematocrit between
45 - 50% were **~4 times** more likely to
die from cardiovascular causes
or major thrombotic events



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Marchioli, R. et al., N Engl J Med. 2013

Real World PV Patient Treatment Data Suggests HCT Control as Pressing Need

Evaluation of More Than 25,000 PV Patients

Treatment patterns

- Predominant treatment to control HCT is phlebotomy, regardless of patients' risk
- Hydroxyurea is the most common cytoreductive agent, often used in combination with phlebotomy
- Jakafi and interferons are typically used later-line to control multiple cell lines

Hematocrit management

- **Patients are not managed to NCCN guidelines, which recommend maintenance of HCT <45%**
- Nearly half of all patients had at least one HCT test >50%
- Less than 25% of patients had all HCT tests within guideline-recommended limits

Thrombotic risks and events

- **More than 15% of patients experienced a thrombotic event (TE) after treatment initiation**
- For patients with a prior thrombotic event, ~40% had at least one other TE while on treatment
- Stroke was the most commonly occurring TE

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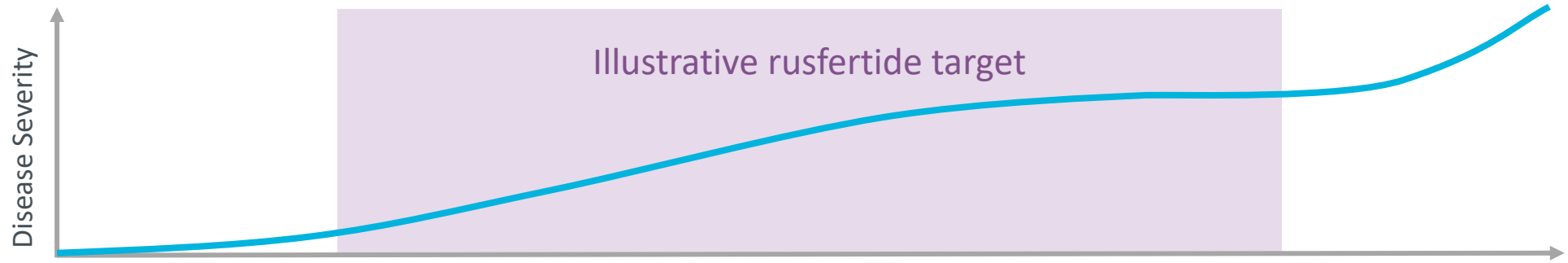
Symphony Patient Journey Data, August 2020; ASH Dec 2020
Data reflects 28,306 patients treated in 2018-2019. HCT data available in a subgroup of 4,246 patients.

Polycythemia Vera

Current Treatment Options and Potential Commercial Opportunity



Disease Stage PV population	**Early / low burden** ~20% of PV population	**Moderate burden** ~60% of PV population	**Late / high burden** ~20% of PV population
Current treatment	Infrequent Phlebotomy (<4/year)	Frequent Phlebotomy +/- HU Besremi*	Besremi* Jakafi**
Treatment goals and considerations	• Maintain HCT ≤ 45% • HCT control may be erratic with up and down excursions from 45% • Can lead to iron deficiency	• Recommended when HCT cannot be controlled, when WBCs/platelets are elevated, or in high-risk patients • Potential long-term side effects • Some patients reluctant to use chemotherapeutic agents	• Excessive WBCs/platelets signal advanced disease • Jakafi is approved for HU resistant/intolerant patients • Jak inhibitors are associated with potential long-term side effects • Besremi has a black box warning

*Newly FDA approved, undergoing U.S. commercial launch; uncertain place in the therapeutic paradigm at present
**~5,300 patients treated with Jakafi; uncertain of Besremi population due to recent approval

PN-235: IL-23 Receptor Antagonist

Oral Targeted Investigational Therapy for Psoriasis and IBD indications

Oral, IL-23 Receptor Specific Peptide Antagonist: PN-235

Janssen Partnership

Objective

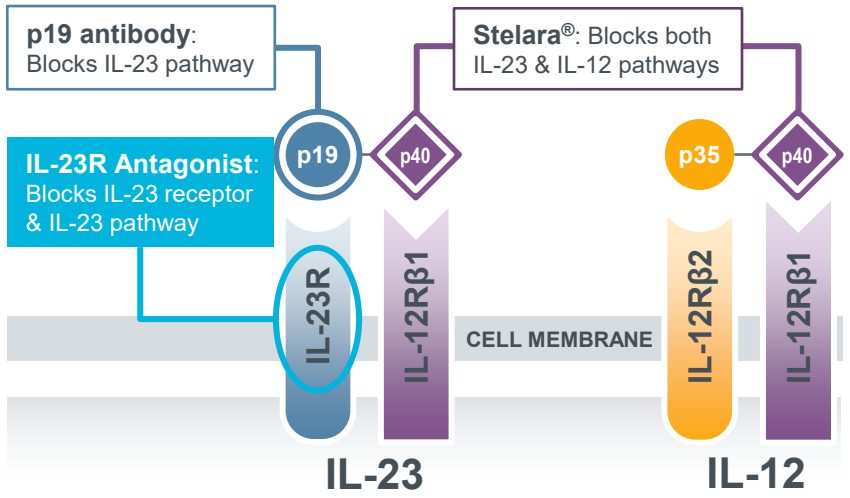
- Extend the Stelara® and Tremfya® franchise and transition from injectable to oral targeted therapy
  - Stelara® and Tremfya® together generated more than $11.26B in total global sales in 2021[1]

Terms

- May 2017: Partnership initiated
- $112.5M in upfront and development milestones received to date
- Eligible for about additional $855M in milestones, up to double digit royalties, US co-detailing rights
  - Study initiation milestones: $25M (psoriasis, received April 2022)

Status

- Focus on the PN-235 candidate, with its superior potency and PK/PD profile, for IBD and non-IBD indications
  - **PN-235 (JNJ-77242113):** Ph1 completed in 2021
  - ***Advancing in plaque psoriasis indication in 240 patient Ph2b FRONTIER 1 study, FRONTIER 2 (long term extension), 80 patient Ph2 SUMMIT study, 27 patient Ph1 study in Japanese/Chinese NHVs***
  - ***Ph2 study initiations in IBD indications expected in 2023***



Stelara® and Tremfya ® are a key Janssen franchise

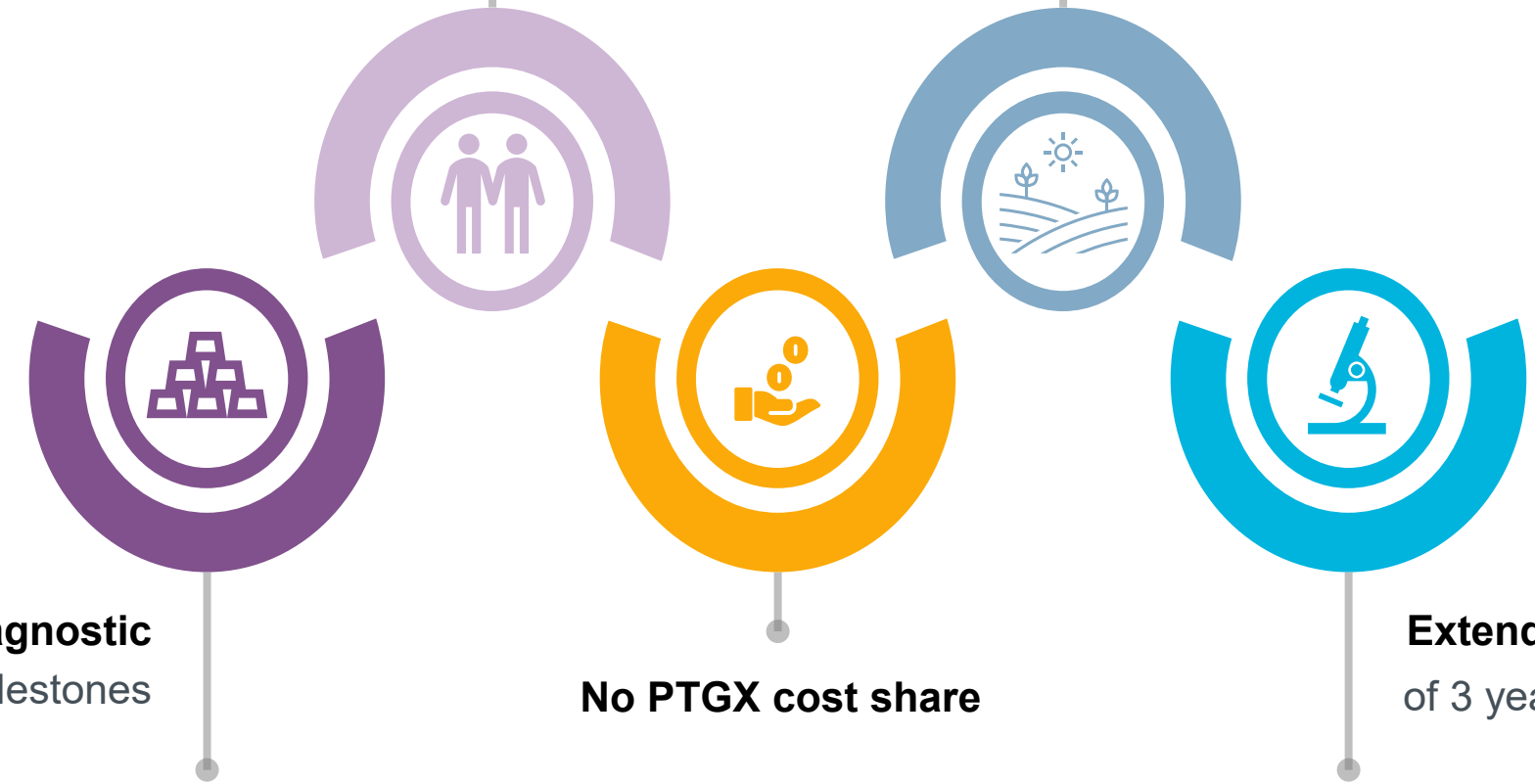
- More than 11.26B total global sales in 2021

[1]Johnson & Johnson 2021 Annual Report. Per the Report, Stelara generated $9.134B in sales; Tremfya generated $2.127B in sales.

Additional Key Aspects of the Janssen-Protagonist Collaboration

Multiple studies
of PN-235

A range
of IL-23 pathway indications



Indication agnostic
development milestones

No PTGX cost share

Extended research term
of 3 years for Janssen

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Milestones Status and Outlook

2023

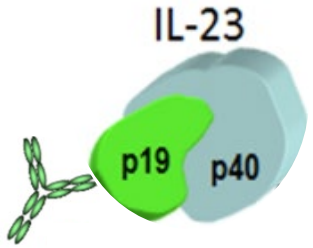
$112.5m **in development milestones have been achieved**

$855m **approximate amount of total future development and sales milestones for which Protagonist remains eligible**

For the near term, the Company is eligible for a **$10 million** milestone payment in connection with the start of a second indication-based Phase 2 study, and a **$50 million** milestone upon dosing of a third patient in a Phase 3 study of PN-235.

Selective blockade of IL-23 signaling by targeting p19

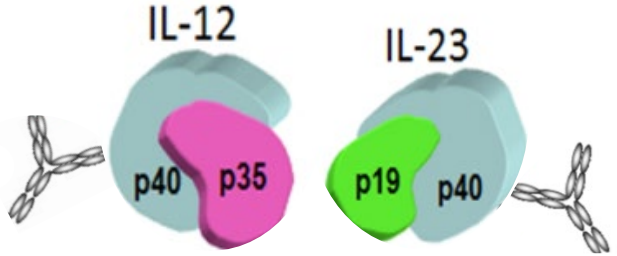
Guselkumab
Tildrakizumab
Risankizumab
Mirikizumab



Targeting IL-23p19; blocks IL-23

- Th17 pathway inhibition

Ustekinumab



Targeting p40; blocks both IL-12 & IL-23

- Inhibits both Th1 and Th17 pathways

PN-235 Rationale

Background Context

Blockade of the IL-12 and IL-23 pathways, as well as the downstream Th17 pathway, have resulted in unprecedented efficacy in psoriasis

- There is intense interest in oral IL-23 inhibitors to replace biologics
- JAK inhibitors have black box warnings; Tyk2 inhibitors have potential safety issues
- The safety profile of blocking the IL-23 pathway is remarkably favorable
- Janssen and Protagonist are developing the only oral IL-23 receptor antagonist with best-in-class potential

The safety and efficacy of selective inhibition of IL-23 is the approach that will provide the most benefit across inflammatory diseases like psoriasis and IBD.

The development of a selective oral IL-23 pathway inhibitor like PN-235 could be a best-in-class approach in the IL-12/23/Th17 pathways.

A Safe & Efficacious Oral Medicine Would Revolutionize Therapeutic Options

Access new patients and diseases

- Enables access to more patients globally
- Expands to more moderate stages of disease
- Solves the issue of patient injection fatigue

Enable novel combinations

- Opens potential option of oral drug as maintenance after biologic induction
- Could serve as a flexible add-on to biologics targeting distinct pathways: e.g., anti-TNFs

The robust collection of studies currently underway—FRONTIER 1, FRONTIER 2, SUMMIT, and more—will shed light on the viability of our oral option and its promise for patients

Protagonist Executive Leadership Team and Financials

Protagonist Team

Experience & Expertise in Drug Discovery, Clinical Development, and Commercialization

Dinesh Patel, PhD	President & CEO
David Liu, PhD	Chief R&D Strategy Officer
Arturo Molina, MD, MS	Chief Medical Officer
Samuel Saks, MD	Clinical Development Advisor
Suneel Gupta, PhD	Chief Development Officer
Asif Ali	Chief Financial Officer
Matthew Gosling	EVP, General Counsel
Mohammad Masjedizadeh, PhD	EVP, Chief Technical Officer
Scott Plevy, MD	EVP & Therapeutic Area Head
Ashok Bhandari, PhD	EVP, Chief Drug Discovery & Preclinical Development Officer
Craig Ostroff, PharmD., R.Ph.	Interim Head of Regulatory Affairs
Abha Bommireddi, MS	SVP, Program Management
Carter King, MBA	SVP, Business Development
Nishit Modi. PhD, MBA	SVP, Clinical Pharmacology
Sarita Khanna, PhD	SVP, Biometrics

Protagonist Therapeutics

Financial Highlights

Financial Resources Forecast Extends Through Full Year 2024*

$267.4M	2024	49.2M
CASH & SECURITIES as of Sept. 30, 2022	**CASH & SECURITIES** provide financial resources forecast through full year 2024*	**SHARES OUTSTANDING** as of Sept. 30, 2022

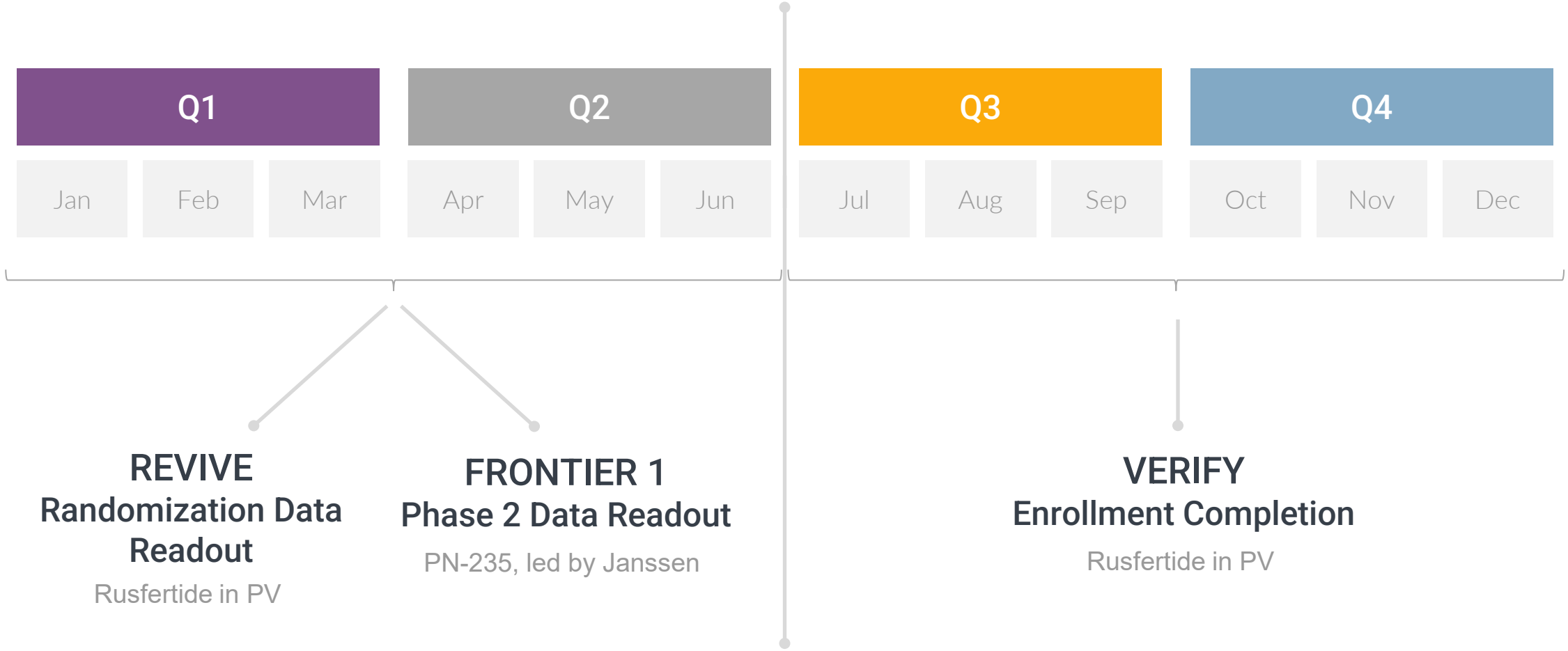
**Based on our current operating plan and expenditures.These estimates may change as new events occur and additional information is obtained.*

Protagonist Therapeutics

Major catalysts ahead

2023 stands to be a transformative year for Protagonist, with two key events in view

Key events in 1H and 2H 2023 (estimated):



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Thank you