COMPANY OVERVIEW

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President & CEO

August 03, 2023
Forward-looking Statements

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Protagonist Therapeutics
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 - Ph3
JNJ-2113 – Ph2b
(formerly PN-235)

Heme Franchise
Oral Peptides

Discovery & pre-clinical
development against new targets
in hematology and immunology
## Product Portfolio

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

<table>
<thead>
<tr>
<th>Programs</th>
<th>Discovery/Pre-Clinical</th>
<th>Phase 1</th>
<th>Phase 2</th>
<th>Phase 3</th>
<th>Key Milestones</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>HEMATOLOGY &amp; BLOOD DISORDERS</strong></td>
<td></td>
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<tr>
<td>Hepcidin Mimetic</td>
<td>POLYCYTHEMIA VERA (PV)</td>
<td></td>
<td></td>
<td>Ph2 elevated Hct (&gt;48%)</td>
<td>PACIFIC: 52-wk open-label study completed</td>
</tr>
<tr>
<td>Rusfertide (PTG-300)</td>
<td></td>
<td></td>
<td>Ph2 REVIVE</td>
<td>Ph3 VERIFY</td>
<td>• REVIFY: ~250 patient, double-blind, placebo-controlled, Enrollment completion 1Q 24</td>
</tr>
<tr>
<td></td>
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<td></td>
<td></td>
<td></td>
<td>• REVIVE: 70 patient randomized withdrawal completed, OLE ongoing</td>
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<tr>
<td>POLYCYTHEMIA VERA (PV)</td>
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<td></td>
<td></td>
<td></td>
<td>• PACIFIC: 52-wk open-label study completed</td>
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<tr>
<td><strong>INFLAMMATORY &amp; IMMUNOMODULATORY DISEASES</strong></td>
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<tr>
<td>Undisclosed Target</td>
<td>Hematology</td>
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<td></td>
<td>• Discovery hits/leads</td>
</tr>
<tr>
<td>Undisclosed Target</td>
<td>Immunology</td>
<td></td>
<td></td>
<td></td>
<td>• Discovery hits/leads</td>
</tr>
<tr>
<td>Oral IL-23R Antagonist (Partnered)</td>
<td>PSORIASIS</td>
<td></td>
<td></td>
<td>Ph3 trial (planned)</td>
<td>• FRONTIER 1 &amp; 2: 255-patient psoriasis study completed, LTE Ongoing</td>
</tr>
<tr>
<td>JNJ-2113 (PN-235)</td>
<td></td>
<td></td>
<td>Ph2b FRONTIER-1 &amp; -2</td>
<td></td>
<td>• Psoriasis Ph3: Study initiation planned</td>
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<td></td>
<td></td>
<td></td>
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<td></td>
<td>• SUMMIT: 90 patient psoriasis delayed release formulation study completed</td>
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<td></td>
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<td></td>
<td>Ph2a SUMMIT</td>
<td>Ph3 trial (planned)</td>
<td>• UC Ph2b: Study initiation planned 4Q 23</td>
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</tbody>
</table>

*New Information*
## Major Catalysts Ahead

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

<table>
<thead>
<tr>
<th>Program</th>
<th>2023: 2H</th>
<th>2024: Q1</th>
<th>Q2</th>
<th>Q3</th>
<th>Q4</th>
<th>2025</th>
<th>2026</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rusfertide in PV</td>
<td>ASH</td>
<td>Ph3 Enrolment completion</td>
<td>EHA</td>
<td>REVIVE Ph3 32 wk 1° end point</td>
<td>NDA filing</td>
<td>Product launch</td>
<td></td>
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<tr>
<td>JNJ-2113 Janssen</td>
<td>Ph2b UC Study initiation</td>
<td>Ph3 Psoriasis clinical program</td>
<td></td>
<td></td>
<td>NDA filing for psoriasis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Discovery &amp; Pre-Clinical</td>
<td>Immunology Oral peptide Hematology Injectable or oral</td>
<td>Development Candidate 1</td>
<td>Development Candidate 2</td>
<td></td>
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</table>
Rusfertide (PTG-300): Hepcidin Mimetic

Addressing Unmet Needs in Polycythemia Vera
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\(^{1,2}\)

Rare disease with ~100,000 diagnosed patients in US\(^1\)

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

Treatment goal is to control

\(\text{HCT} < 45\%\)

to minimize TEs, CV events, and death\(^3\)

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1. NORD Rare Disease Database, Polycythemia Vera. https://rarediseases.org/rare-diseases/polycythemia-vera/
Polycythemia Vera
A Blood Disorder with Significant Unmet Needs with Current SOC

1. Maintaining HCT<45% is critical in PV, as per NCCN guidelines

2. Uncontrolled HCT is associated with higher rates of death from cardiovascular causes or thrombotic events
   • Burdensome symptoms including fatigue and concentration problems
     – 84% of patients report fatigue, and 23% report spending full days in bed because of symptoms
   • Impacts patient reported activities of daily living and reduce productivity

3. Real world data shows that up to 78% of patients have uncontrolled HCT with tests >45%
   • Current standard of care (SOC) approaches are inadequate for HCT control and symptoms management

4. There is no available pharmaceutical option with RBC-specific mechanism to target HCT
   • Rusfertide is a mimetic of Hepcidin, the natural hormone regulating iron homeostasis and erythrocytosis

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Current Treatment Options for PV and Potential Limitations

Cytoreductive Therapies May Lead to Intolerance and/or Inadequate Hematocrit Control

**Hydroxyurea**

- **Hydrea®**
  - Typically used as a first-line treatment in high-risk patients
  - Patients still experience periods where HCT $>45\%$, potentially resulting in dose increases and in need for phlebotomies
  - Often discontinued due to blood counts, AEs, disease progression, or poor adherence
  - Risk of skin cancer
  - 25% of patients become resistant or intolerant

**Interferon**

- **Pegasys®, Besremi®**
  - Interferons have long been used off-label in treatment; Besremi is the first interferon product approved for PV
  - Slow onset of action, with a median time to response of 1.2 to 1.4 years
  - Failed to show noninferiority to HU at 12 months in the PROUD-PV study
  - *Black box warning* for serious neuropsychiatric, autoimmune, ischemic, and infectious disorders

**Ruxolitinib**

- **Jakafi®**
  - Only approved for hydroxyurea-resistant or intolerant patients
  - Improves splenomegaly, a potential marker of disease progression
  - Potential serious side effects include thrombocytopenia, neutropenia, and anemia
  - Risk of skin cancer
  - 23% of patients were found to have discontinued ruxolitinib within a mean of 2 years post treatment initiation

---

3. Hydrea FDA label.
Only 22% of PV Patients Have Consistently Controlled Hematocrit

HCT is Not Managed to Guidelines, Regardless of Patients’ Risk Status

![Diagram showing the percentage of patients with controlled and uncontrolled HCT tests.](image)

- **All HCT tests <45%**: 78%
  - 22% Some or All Tests >45%
  - 53% Some HCT tests >50%
  - 37% All HCT tests <50%

- **Of the 78% of uncontrolled patients...**
  - 10% All HCT tests >50%
  - 53% Some HCT tests >50%
  - 37% All HCT tests <50%

Uncontrolled HCT >45% leads to a greater risk of thrombotic events, cardiovascular events, death, and may impact QoL²

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

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

All HU-treated ($P<0.0001$)


PV Market Overview

Rusfertide has the potential to create a new standard of care in PV

- Broad spectrum of patients
- Competition with distinct limitations
- High unmet needs with uncontrolled patients

Prevalent Patients in the U.S.¹

~160,000

Diagnosed & Treated Patients in the U.S.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
Identifying PV Patients with Moderate Treatment Burden

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

Representative events to identify uncontrolled period for a PV patient

**Phlebotomy Frequency**
An increase in frequency of phlebotomies indicates the intervention is not working to maintain HCT

**Dosing Fluctuations**
Dosage fluctuations can signify that there is a need for an altered treatment paradigm. High doses of HU (1-2 g/day) can also indicate difficult-to-control PV

**Treatment Switches**
Switching treatments (between products or interventions) posits that physicians are looking for a more efficacious treatment

**Symptoms**
Patients with symptoms like fatigue and cognitive dysfunction have persistent unmet needs despite current treatment

**Thrombotic Events**
Occurrence of thrombotic events post treatment initiation is an indicator of the ineffectiveness of the treatment - one of the definitive examples of an “uncontrolled” PV patient

Outcome of an uncontrolled phase
Rusfertide, a hepcidin mimetic, can potentially benefit a broad spectrum of patients with moderate disease burden for a major portion of their journey with the disease by functioning as an erythrocytosis specific agent and enabling consistent and continuous control of HCT <45%.
Rusfertide for Polycythemia Vera

Three Clinical Studies Ongoing

- **Ph2 REVIVE** Study (n=70):
  - Clinical updates presented at ASH 2021, ASCO 2022, EHA 2022, ASH 2022
    - Most recent Phase 2 data, presented at ASCO 2022, demonstrates the effects of dosing interruption and resumption
  - Randomized withdrawal study completed

- **Ph2 PACIFIC** Study (n=20):
  - High hematocrit (HCT >48%) 16-week study completed; 52-week open-label study completed in Q2 2023

- **Ph3 VERIFY** Study (n=250):
  - Study execution continues with enrollment completion expected in 1Q 2024
  - Agreed upon Phase 3 VERIFY protocol with the FDA and CHMP (EU)

- Rusfertide has **Orphan Drug** designation and **Fast Track** status
Clinical Study of Rusfertide in PV Patients with High Hematocrit (>48%)

Rapid Hematocrit Control <45% was Achieved

- 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

Median time to first HCT <45%: 4.93 wks
Rate of Hct Reduction: 1.7%/wk
Proportion <45% Prestudy: 0%
Proportion of Patients <45% at Wk 16: 69%
Phase 2 Study of Rusfertide in PV Patients (REVIVE)

**GOAL:** Maintain Hematocrit <45%

**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 subcutaneously, added to prior standard therapy

**KEY ENDPOINTS:**
- Safety
- Maintain Hematocrit <45%
- Responder analysis
- Reduction in Phlebotomies
- Symptom Scores: MPN-SAF TSS

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1 As of May 11, 2023
Baseline Characteristics of Study Participants in REVIVE Study

<table>
<thead>
<tr>
<th>Characteristics (n = 70)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>AGE</strong></td>
</tr>
<tr>
<td>Range</td>
</tr>
<tr>
<td><strong>GENDER</strong></td>
</tr>
<tr>
<td>Females</td>
</tr>
<tr>
<td>Males</td>
</tr>
<tr>
<td><strong>RISK</strong></td>
</tr>
<tr>
<td>Low</td>
</tr>
<tr>
<td>High</td>
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<tr>
<td><strong>DURATION SINCE PV DIAGNOSIS</strong></td>
</tr>
<tr>
<td>&lt;1 yr</td>
</tr>
<tr>
<td>1 - &lt;3 yrs</td>
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<tr>
<td>3 - &lt;5 yrs</td>
</tr>
<tr>
<td>≥5 yrs</td>
</tr>
<tr>
<td><strong>THERAPIES</strong></td>
</tr>
<tr>
<td>PHL only</td>
</tr>
<tr>
<td>PHL + HU</td>
</tr>
<tr>
<td>PHL + IFN</td>
</tr>
<tr>
<td>PHL + RUX</td>
</tr>
<tr>
<td>PHL + Multiple Agents</td>
</tr>
<tr>
<td><strong>NUMBER OF PHL IN 28 WEEKS PRIOR</strong></td>
</tr>
<tr>
<td>2-3</td>
</tr>
<tr>
<td>4-5</td>
</tr>
<tr>
<td>≥6</td>
</tr>
<tr>
<td>Median</td>
</tr>
<tr>
<td><strong>DAYS BETWEEN PHLEBOTOMIES</strong></td>
</tr>
<tr>
<td>Median</td>
</tr>
</tbody>
</table>

Enrollment complete. Data as of March 10, 2022, and as presented at ASCO June 2022
Part 1: Dose Finding and Efficacy Evaluation, Weeks 1-28

Significant Reduction in Phlebotomy Frequency

Phlebotomy Only (n=37)

Phlebotomy + Cytoreductive (n=33)

Data cutoff: Feb 15, 2023
Part 2: Blinded Randomized Withdrawal, Weeks 29-41

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

- **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

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**Highly significant efficacy** in rusfertide arm vs. placebo

Rusfertide

- **69.2%** responders
  - n=18

Placebo

- **18.5%** responders
  - n=5

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*p=0.0003

*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
  - Hematocrit >48%
  - An increase of ≥5% in hematocrit compared to Week 29 pre-randomization hematocrit value
Phase 2 REVIVE Study: Part 1 and 2
Consistent Effects on Freedom from Phlebotomy

Phlebotomy-Free on Rusfertide

<table>
<thead>
<tr>
<th>Rusfertide</th>
<th>Part 1</th>
<th>Part 2</th>
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<tbody>
<tr>
<td>Dose Titration</td>
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<tr>
<td>Open-Label Efficacy</td>
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<tr>
<td>Double-Blind Efficacy</td>
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</tbody>
</table>

- **Part 1**: Dose Titration
  - Wk 1-17 (N=65): 76.9% (n=50)
  - Wk 17-29 (N=63): 87.3% (n=55)

- **Part 2**: Double-Blind Efficacy
  - Wk 29-41 (N=26): 92.3% (n=24)
Phase 2 REVIVE Study: Consistent Efficacy
Rufsertide Significantly Delays Time to Event on Multiple Outcomes Compared to Placebo

Responder

Absence of PHL Eligibility

HCT <45%

P <0.0001

Percent of Subjects vs. Weeks

Placebo (N=27)
Rufsertide (N=26)
Phase 2 REVIVE Study: Symptom Improvement

Improvement in Ferritin Levels and Symptoms

Individual symptoms assessed using MPN-SAF

p-values are based on paired comparisons

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**Symptom Improvements in Part 1 (28 Weeks)**

**Problems with Concentration**

- Baseline (n=18) Week 29 (n=14)
  - Symptom Score: 6.1 vs. 3.0
  - p-value: 0.0018

**Itching**

- Baseline (n=16) Week 29 (n=12)
  - Symptom Score: 6.2 vs. 3.3
  - p-value: 0.0054

**Fatigue**

- Baseline (n=25) Week 29 (n=20)
  - Symptom Score: 6.0 vs. 4.2
  - p-value: 0.0074

**Inactivity**

- Baseline (n=18) Week 29 (n=12)
  - Symptom Score: 5.8 vs. 3.0
  - p-value: 0.0005

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**Graphs and Data**

- Ferritin levels over time with symptom improvements.
- Bar charts showing symptom scores before and after treatment.
- Comparison of symptom scores between baseline and Week 29, highlighting improvements.

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**Legend**

- Screening
- Part 1 – Dose Finding
- Part 3 – Open Label Extension

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**Protagonist Therapeutics**

23
Phase 2 REVIVE Study: Safety and Exposure

Rusfertide Was Generally Well Tolerated

- 70 subjects were enrolled in the rusfertide REVIVE study
  - 52 subjects (74.3%) have exposure ≥ 1 yr
  - 32 subjects (45.7%) have exposure ≥ 1.5 yrs
  - 10 subjects (14.3%) have exposure ≥ 2 yrs
  - 3 subjects (4.3%) have exposure ≥ 2.5 yrs

- Rusfertide was generally well tolerated
  - A majority of TEAEs were Grade 1 or 2
    - There were no Grade 4 or 5 TEAEs
  - Most common TEAEs were injection site reactions (ISR)
    - Events were localized, Grade 1 or 2 in severity, and generally did not lead to treatment discontinuation
    - ISRs decreased in incidence with continued treatment
  - Symptoms associated with PV such as fatigue, pruritus, headache, and dizziness were the second most common reported AEs
  - Two events related to treatment with rusfertide led to discontinuation (mild thrombocytosis and recurrent grade 1 injection site erythema)

### TEAEs by Preferred Term Noted at ≥15%

<table>
<thead>
<tr>
<th>TEAE by Preferred Term</th>
<th>N=70</th>
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</thead>
<tbody>
<tr>
<td>Subjects with at least one TEAE</td>
<td>70 (100%)</td>
</tr>
<tr>
<td>Injection site erythema</td>
<td>45 (64.3)</td>
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<tr>
<td>Injection site pain</td>
<td>29 (41.4)</td>
</tr>
<tr>
<td>Injection site pruritus</td>
<td>28 (40.0)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>22 (31.4)</td>
</tr>
<tr>
<td>Injection site mass</td>
<td>18 (25.7)</td>
</tr>
<tr>
<td>Pruritus</td>
<td>18 (25.7)</td>
</tr>
<tr>
<td>Arthralgia</td>
<td>17 (24.3)</td>
</tr>
<tr>
<td>Injection site swelling</td>
<td>17 (24.3)</td>
</tr>
<tr>
<td>Dizziness</td>
<td>16 (22.9)</td>
</tr>
<tr>
<td>Headache</td>
<td>16 (22.9)</td>
</tr>
<tr>
<td>Nausea</td>
<td>16 (22.9)</td>
</tr>
<tr>
<td>Anemia</td>
<td>14 (20.0)</td>
</tr>
<tr>
<td>COVID-19</td>
<td>14 (20.0)</td>
</tr>
<tr>
<td>Injection site irritation</td>
<td>13 (18.6)</td>
</tr>
<tr>
<td>Injection site bruising</td>
<td>11 (15.7)</td>
</tr>
</tbody>
</table>

Data as of 15 February 2023
Phase 2 REVIVE Study: Overall Safety

No New Safety Signals

- 18.6% subjects reported an SAE
- A total of 7 subjects diagnosed with malignancy after starting the study
  - All 7 subjects had risk factors before exposure to rusfertide including pre-malignant lesions, history of cancer, or prior cytotoxic and/or cytoreductives
  - 5 out of 7 subjects had a prior malignancy
  - Most common event during the study was in situ or stage I non-melanoma skin cancer (NMSC)
  - Out of 7 subjects, only 2 have been identified since restarting rusfertide dosing in Dec 2021, after implementing mandatory dermatologic exams

<table>
<thead>
<tr>
<th>Category</th>
<th>Event</th>
<th>Subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subjects with at least one Serious Adverse Event</td>
<td>13 (18.6%)</td>
<td></td>
</tr>
<tr>
<td>Cardiac</td>
<td>Myocardial Infarction</td>
<td>1 (1.4%)</td>
</tr>
<tr>
<td></td>
<td>Atrial fibrillation</td>
<td>1 (1.4%)</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>Constipation</td>
<td>1 (1.4%)</td>
</tr>
<tr>
<td></td>
<td>Anogenital Dysplasia</td>
<td>1 (1.4%)</td>
</tr>
<tr>
<td>General</td>
<td>Non-cardiac chest pain</td>
<td>1 (1.4%)</td>
</tr>
<tr>
<td>Infections</td>
<td>Gastroenteritis</td>
<td>1 (1.4%)</td>
</tr>
<tr>
<td>Neoplasms</td>
<td>Basal cell carcinoma</td>
<td>3 (4.3%)</td>
</tr>
<tr>
<td></td>
<td>Malignant Melanoma</td>
<td>2 (2.9%)</td>
</tr>
<tr>
<td></td>
<td>AML</td>
<td>1 (1.4%)</td>
</tr>
<tr>
<td></td>
<td>Squamous cell carcinoma</td>
<td>1 (1.4%)</td>
</tr>
<tr>
<td>Nervous</td>
<td>Cerebrovascular accident</td>
<td>1 (1.4%)</td>
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<tr>
<td></td>
<td>Syncope</td>
<td>1 (1.4%)</td>
</tr>
<tr>
<td></td>
<td>Transient Ischemic Attack</td>
<td>1 (1.4%)</td>
</tr>
<tr>
<td>Vascular</td>
<td>Peripheral artery aneurysm</td>
<td>1 (1.4%)</td>
</tr>
<tr>
<td></td>
<td>Peripheral vascular disorder</td>
<td>1 (1.4%)</td>
</tr>
</tbody>
</table>

Data as of 15 February 2023
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, December 2022; no new safety signals observed

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

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

**Ongoing Study of N~250 Subjects**

**Ph3 study design capitalizes on the successful outcome to date of the Ph2 REVIVE Study**

---

**Part 1a**

- **Double Blind**
  - Dose Titration (Weeks 0-20)
  - Primary Efficacy (Weeks 20-32)

**Part 1b**

- Durability of Response (Weeks 32-52)

---

**Screening** (Up to 4 Weeks)

**Rusfertide + Ongoing Therapy (n~125)**

**Placebo + Ongoing Therapy (n~125)**

- Week 0
  - Randomize (1:1)

- Week 32
  - 1° EP: phlebotomy free
  - 2° EPs: # phlebotomies, symptoms, etc.

- Week 52
  - Durability of Response

---

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.
Clinical Study of Rusfertide in Patients with Hereditary Hemochromatosis

Control Serum Iron and Reduce Phlebotomies

- 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 accepted for publication in notable scientific journal
  - Rusfertide treatment rapidly reduced and suppressed serum iron and TSAT.
  - Essential elimination of phlebotomies and stable LIC.
  - Rusfertide was generally well tolerated
JNJ-2113 (formerly PN-235): IL-23 Receptor Antagonist

Oral Targeted Investigational Therapy for Psoriasis and Other IL-23 Mediated Diseases
Protagonist-Janssen Oral, IL-23R Antagonist Collaboration

Collaboration overview
- Initiated in 2017 with I&I market leader Janssen Biotech¹
- JNJ-2113 (formerly PN-235) jointly discovered using Protagonist’s proprietary peptide discovery platform
  - Protagonist completed pre-clinical and Phase 1 studies
  - Janssen responsible for further development and commercialization

Collaboration economics
- Protagonist eligible for up to $855M in development and sales milestones and upward-tiering royalties for JNJ-2113 and other collaboration compounds

Recent clinical data; development status
- Phase 2B FRONTIER 1 data presented at WCD 2023 (July 2023)
- Phase 3 psoriasis study planned (early 2024)
- Phase 2b UC study planned (Q4 2023)

JNJ-2113 potential best-in-class oral agent
- Potential to expand IL-23 market to oral therapy

IL-23R Antagonist Market Overview
Multi-billion Market Opportunity for an Oral Agent

Significant market potential for IL-23R antagonist
- Relevant indications include psoriasis, psoriatic arthritis, IBD (ulcerative colitis, Crohn’s disease)
- Psoriasis prevalence = 125M WW patients\(^1\) (8M US\(^1\))
  - 30% develop psoriatic arthritis
- $13.2B major market sales for psoriasis (2020)\(^2\)
  - Projected growth to $25.3B in 2030\(^2\)
- $14.2B major market sales for IBD (2020)\(^2\)
  - Projected growth to $24.9B in 2029\(^2\)

Oral agents expected to contribute to market growth
- Substantial portion of patients untreated with current standard of care
  - 25% of treated psoriasis patients treated with biologics\(^1\)
- Despite strong efficacy, biologics associated with safety concerns, loss of response, inconvenient administration, highlighting the need for safe and effective oral options\(^3, 4\)

JNJ-2113 Characteristics

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

- Highly potent (single digit picomolar) oral IL-23R antagonist:
  - >1000-fold more potent vs first-generation candidate (PBMC, phospho-STAT3 assay)
  - Similar or better target affinity vs. IL-23 mAbs

- High oral stability:
  Ex-vivo stability: >24hr half-life in feces (human, cyno, and rat)
  In-vivo stability: >25% fecal recovery after 24hrs in cynos

- Pre-clinical Proof-of-Concept:
  - Achieved pre-clinical PoC with oral dosing in IL-23-induced rat ear skin inflammation model
  - Similar inhibition to systemic IL-23 mAbs

- Phase 1 study in NHVs:
  - Inhibition of IL-23 pathway related biomarkers comparable to approved IL-23 mAbs

- Phase 2b FRONTIER1 study in Psoriasis:
  - Potential for best-in-class oral agent for psoriasis
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.
Phase 1 Study of JNJ-2113 in Healthy Volunteers

Safety, Pharmacokinetics, Systemic Pharmacodynamics

- 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.
### 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

#### Study Design

<table>
<thead>
<tr>
<th>Screening (Up to 4 Weeks)*</th>
<th>Treatment (Weeks 0-16)</th>
<th>Safety Follow-up (4 Weeks)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Dose 1 QD &amp; Placebo</td>
<td>LTE (FRONTIER 2) or 4 weeks safety follow-up</td>
</tr>
<tr>
<td>2</td>
<td>Dose 2 QD &amp; Placebo</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Dose 3 QD &amp; Placebo</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>Dose 1 BID &amp; Placebo</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>Dose 3 BID &amp; Placebo</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>Placebo</td>
<td></td>
</tr>
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</table>

*Week 0 Randomize

Week 16 Primary Endpoint
## Demographics and Disease Characteristics at Baseline

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

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.
**JNJ-2113 Phase 2B Frontier 1 Data**

### Dose Response

- Clear, linear dose-response
- Once daily dosing appears more efficacious in comparison to twice daily dosing
Cross-Study Comparison of JNJ-2113 to Clinically Relevant Phase 2 Benchmarks

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%)
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%)
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%)
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.
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

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

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

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

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

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.

Most frequently reported AEs were COVID-19 and nasopharyngitis

There was no evidence of a dose-dependent increase in the occurrence of abnormalities.
JNJ-2113 (formerly PN-235):

Conclusions from FRONTIER 1 Phase 2b PsO Study and Next Steps

JNJ-77242113 is a first-in-class oral IL-23R antagonist peptide that demonstrated significantly greater efficacy compared with placebo in patients with moderate-to-severe plaque PsO across all doses in a Phase 2b study.

A dose response in PASI scores (75, 90, 100) was demonstrated.

JNJ-77242113 was well tolerated at all doses with numbers of AEs comparable to the placebo group. No dose dependent relationship in AEs or lab abnormalities was observed.

JNJ-77242113 holds promise as an effective oral therapy with biologic-like efficacy and safety in moderate to severe plaque psoriasis.

The FRONTIER 1 results support further development of JNJ-77242113 in phase 3 studies in psoriasis as well as other IL-23 mediated disease indications.

Next Steps

- Phase 3 study in psoriasis by early 2024
  - QD dosing with immediate release formulation, informed by Ph2b results
- Phase 2b study in ulcerative colitis in Q4 2023

JNJ-2113 is a potential best, first-, and only-in-class oral IL-23 receptor antagonist.
Janssen SUMMIT Phase 2a Plaque Psoriasis (PsO) Study Design

Delayed Release QD Tablets

Adult Patients with PP
N=90

Eligibility:
• Moderate – Severe PP

Inclusion:
• BSA ≥ 10%
• PASI ≥ 12

Primary endpoint:
• PASI ≥ 75 at Week 16

Screening
(Up to 4 Weeks)*

Treatment
(Weeks 0-16)

Safety Follow-up
(4 Weeks)

1
Dose 1 qd

2
Dose 2 qd

3
Placebo qd

Week 0
Randomize

Week 16
Primary Endpoint

Study completed April 10, 2023
Janssen Milestones Status and Outlook
2023 and Beyond

$112.5m
Upfront and development milestones that have been achieved

$855m
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

<table>
<thead>
<tr>
<th>Indication</th>
<th>Milestone</th>
<th>Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st indication, Psoriasis</td>
<td>Ph3 initiation</td>
<td>$50M</td>
</tr>
<tr>
<td></td>
<td>Ph3 1° end point achieved</td>
<td>$115M*</td>
</tr>
<tr>
<td></td>
<td>NDA filing</td>
<td>$35M*</td>
</tr>
<tr>
<td></td>
<td>NDA approval</td>
<td>$50M*</td>
</tr>
<tr>
<td>2nd indication, UC</td>
<td>Ph2 initiation</td>
<td>$10M</td>
</tr>
<tr>
<td></td>
<td>Ph3 initiation</td>
<td>$15M</td>
</tr>
</tbody>
</table>

* $200M milestones associated with successful Ph3 study, NDA filing and approval, are NOT included in current cash runway forecast through end of 2025
Financial Highlights

Financial Resources Forecast Extends Through Full Year 2025

- **$313.4M**
  - Cash, Cash Equivalents & Marketable Securities as of June 30, 2023
  - Provide financial resources forecast through full year 2025

- **2025**

- **~57.5M**
  - Shares Outstanding as of June 30, 2023
Thank you