COMPANY OVERVIEW

Dinesh V. Patel, PhD
President & CEO

December 2021
Forward-looking Statements

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A Clinical Development Stage Biotechnology Company
Discovering and Developing Novel Peptide Therapeutics
to Address Unmet Medical Needs
in Both Rare and Common Diseases
Novel Peptide Assets to Address Unmet Needs in Rare and Prevalent Diseases

Innovative Peptide Technology Platform

1. Computational
   Vectrix, Clusters
   Vectrix® Clusters

2. Phage Libraries
   Hits

3. Peptide Chemistry
   SAR, Leads

4. Oral Stability
   Peptidomimetics
   GI Assays

5. GI-Restricted
   Targeted GI absorption & delivery

6. Systemic Availability
   Formulation
   SAR, Transport

Clinical Assets
- Rusfertide
- PN-943
- PN-235
- PTG-100

Rare Blood Diseases

GI Diseases, IBD
## Product Portfolio

### Multiple Development Candidates in Multiple Indications

<table>
<thead>
<tr>
<th>Programs</th>
<th>Candidate</th>
<th>Study</th>
<th>Phase 1</th>
<th>Phase 2</th>
<th>Key Milestones</th>
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<tbody>
<tr>
<td><strong>Hematology &amp; Blood Disorders</strong></td>
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<tr>
<td>Hepcidin Mimetics</td>
<td>rusfertide (PTG-300)</td>
<td>300-11</td>
<td>Polycythemia Vera (PV)</td>
<td>PV Ph2 PoC trial</td>
<td>PV Ph3</td>
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<td></td>
<td>s.c.</td>
<td>300-04</td>
<td>PV Ph2 PoC trial</td>
<td>PV Ph2 in Patients with Elevated Hematocrit</td>
<td>• Resuming enrollment</td>
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<tr>
<td></td>
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<td>300-08</td>
<td></td>
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<td>• Data updates at EHA &amp; ASH 2021</td>
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<td></td>
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<td>300-06</td>
<td>Hereditary Hemochromatosis (HH)</td>
<td></td>
<td>• Resuming dosing into OLE</td>
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<td></td>
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<td>Ph2 PoC</td>
<td>• Data presentation at ASH 2021</td>
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<td>• Study completed; clinical PoC established</td>
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<td>• Data presentation at AASLD and ASH 2021</td>
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<tr>
<td><strong>Inflammatory &amp; Immunomodulatory Diseases</strong></td>
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<td>Oral GI Restricted a4b7-Integrin Antagonists</td>
<td>PN-943</td>
<td>IDEAL</td>
<td>Ulcerative Colitis (UC) Ph2 PoC</td>
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<td>• 150 patient study</td>
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<td>Oral IL-23R Antagonists</td>
<td>PN-235</td>
<td>Ph1 in NHVs</td>
<td></td>
<td></td>
<td>• Topline data in Q2 2022</td>
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<td>Psoriasis Ph2</td>
<td></td>
<td>• Ph1 Completed</td>
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<td>Initiation in early 2022</td>
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<td>IBD Ph2</td>
<td></td>
<td>Initiation in 2H 2022</td>
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Rusfertide (PTG-300): HEPCIDIN MIMETIC
To Potentially Address Unmet Needs in Both Rare & Common Diseases
Rusfertide for Polycythemia Vera

Overview of Current Status and Recent Progress

• Orphan, Fast Track and Breakthrough designations
• Clinical update presented at ASH 2021
• New IB and ICF, enhanced safety surveillance measures and inclusion/exclusion criteria following brief (21-day) clinical hold. Enrollment and dosing have resumed.
• Clinical studies
  − Phase 2 randomized withdrawal study has resumed enrollment; data updates provided at EHA and ASH 2021
  − Phase 2 PV study with elevated hematocrit (48% or higher) has resumed dosing into open-label extension; data presented at ASH 2021
  − Regulatory interactions continue to finalize and enable Phase 3 study initiation in Q1 2022; Phase 3 design presented at ASH 2021

Rusfertide (PTG-300)

Potential for managing hematocrit per NCCN guidelines without creating iron deficiency, while improving symptoms

Close consultation underway w/ regulators

Potential as a first natural hormone mimetic therapy for PV

Continued Progress Underway

• Orphan, Fast Track and Breakthrough designations
• Clinical update presented at ASH 2021
• New IB and ICF, enhanced safety surveillance measures and inclusion/exclusion criteria following brief (21-day) clinical hold. Enrollment and dosing have resumed.
• Clinical studies
  − Phase 2 randomized withdrawal study has resumed enrollment; data updates provided at EHA and ASH 2021
  − Phase 2 PV study with elevated hematocrit (48% or higher) has resumed dosing into open-label extension; data presented at ASH 2021
  − Regulatory interactions continue to finalize and enable Phase 3 study initiation in Q1 2022; Phase 3 design presented at ASH 2021
Rusfertide Featured at ASH 2021 Presentations and CME Sponsored Event

Oral Presentations

- "Rusfertide (PTG-300) Controls Hematocrit Levels and Essentially Eliminates Phlebotomy Requirement in Polycythemia Vera Patients"
  Session 634. Myeloproliferative Syndromes

- "Rusfertide (PTG-300) Induction Therapy Rapidly Achieves Hematocrit Control in Polycythemia Vera Patients without the Need for Therapeutic Phlebotomy"
  Session 634. Myeloproliferative Syndromes

Poster Presentations

- "A Phase 3 Study of the Hepcidin Mimetic Rusfertide (PTG-300) in Patients with Polycythemia Vera"
  Session 634. Myeloproliferative Syndromes

- "Regulation of Iron Homeostasis and Efficacy of Rusfertide Analog Peptide in a Mouse Model for Polycythemia Vera"
  Session 102. Iron Homeostasis and Biology

- "Rusfertide (PTG-300), a Hepcidin Mimetic, Maintains Liver Iron Concentration in the Absence of Phlebotomies in Patients with Hereditary Hemochromatosis"
  Session 102. Iron Homeostasis and Biology

Friday Night CME Symposium

- “Diagnosis and Treatment of PV Where Are We and Where Are We Going?”
  Hyatt Regency Atlanta
Polycythemia Vera

Disease Background

Myeloproliferative neoplasm characterized by excessive production of red blood cells (RBCs)
- Characterized by Janus Kinase 2 (JAK2) mutation

Serious chronic condition
- Rare disease: ~100,000 diagnosed patients in USA
- Diagnosed commonly in individuals 50-70 years of age
- Median survival ~20 years
- Thrombotic and cardiovascular risks; may progress to myelofibrosis or leukemia

Treatment goal is to control hematocrit level <45%
- Elevated hematocrit is a hallmark of the disease
- Maintaining hematocrit <45% is critical to minimizing thrombosis, CV events, and death
Polycythemia Vera

Disease, Diagnosis, Prevalence, Treatment Goal

- PV patients are treated with periodic therapeutic phlebotomy (TP) +/- cytoreductive therapy to maintain hematocrit levels <45%.

- Despite current available therapies, PV patients likely spend significant time with hematocrit levels >45%, thereby potentially increasing their risk of thrombosis (Marchioli et al, NEJM 2013).

- The goal of TP is to generate iron deficiency which is thought to be needed to dampen PV erythropoiesis but it is thought to contribute to PV associated systemic symptoms due to the depletion of iron stores in non-hematopoietic tissues.

- PV as compared to secondary forms of erythrocytosis is associated with relative suppression of hepcidin potentially due to greater degrees of expanded erythropoiesis and iron deficiency (Ginzburg / Hoffman Leukemia 2018).

- Erythrocytosis in PV occurs despite iron-deficient erythropoiesis.
Polycythemia Vera
Current Treatment Options

**Phlebotomy**
- Treatment goal is to maintain HcT ≤ 45%
- HcT control may be erratic with up and down excursions from 45%
- Can lead to iron deficiency

**Hydroxyurea +/- Phlebotomy**
- Recommended when HcT cannot be controlled, or in high-risk patients
- Potential long-term side effects
- Some patients reluctant to use chemotherapeutic agents

**Besremi* (ropoeginterferon alfa-2b-njft) injection**
- Approved for HU resistant/intolerant patients
- ~5,300 patients/yr treated
- ~25% develop intolerance or resistance
- Potential side effects include cytopenia

**Jakafi**

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*NEW FDA approved, undergoing U.S. commercial launch; uncertain place in the therapeutic paradigm at present
1. MPN Landmark Survey 2017, Trinity Primary Research 2019
Understanding PV Patient Journey

Evaluating the Unmet Need of PV Patients in US

- Evaluation of 28,306 PV patients treated in 2018-2019
- Hematocrit levels: lab tests of 4,264 patients

Key Findings in three categories

- Treatment patterns
- Hematocrit management to NCCN guidelines
- Thrombotic risks and events

Real world PV patient treatment data (2018-2019)¹

- Treated PV Patients
  - N = 28,306
- >2 Hct Lab Tests
  - N = 4,264

¹ Symphony Patient Journey Data Large, representative, and longitudinal source of healthcare claims data that captures over 290MM patients with over 78% of all prescription claims and 60% of all medical claims. Medical, hospital, and prescription history is captured across treatment settings and payers with history back to 2003.
Real World PV Patient Treatment Data

Hematocrit Not Managed to NCCN Guidelines of <45% in Majority of Patients

Treatment patterns
- Predominant treatment is phlebotomy, regardless of risk
- Hydroxyurea is the most commonly used cytoreductive agent
- Combination of hydroxyurea and phlebotomy commonly used to control HcT

Hematocrit management to NCCN guidelines
- Only 22% patients had all HcT tests below 45%
  - In high-risk patients only 25% patients had all HcT test below 45%
  - 60% of these high-risk patients initiated treatment on phlebotomy vs 31% on HU, and the majority of patients never switched therapies

Thrombotic risks and events
- For patients with a prior thrombotic event, ~40% had at least another TE while on treatment
  - For patients without prior thrombosis, ~10% had at least one TE while on treatment
Real World PV Patient Treatment Data
Understanding Current Treatment Regimens and Unmet Need of PV Patients in US

- Predominant treatment is phlebotomy regardless of risk
- Hydroxyurea is the most commonly used cytoreductive agent
- Combination of hydroxyurea and phlebotomy commonly used to control HcT

*Jakafi is approved for HU resistant/intolerant PV population

1 Symphony Patient Journey Data Large, representative, and longitudinal source of healthcare claims data that captures over 290MM patients with over 78% of all prescription claims and 60% of all medical claims. Medical, hospital, and prescription history is captured across treatment settings and payers with history back to 2003
Real World PV Patient Treatment Data

Hematocrit Not Managed to NCCN Guidelines of <45% in Majority of Patients

- Only 22% patients had all HcT tests below 45%
  - 78% patients had at least one test at ≥45% HcT
- Almost half had HcT >50% at least once during observation period

*Patient HcT groups are mutually exclusive

Hematocrit (HcT)

<table>
<thead>
<tr>
<th>Patient Group</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>HcT Tests Above 50%</td>
<td>49%</td>
</tr>
<tr>
<td>HcT Tests Under 50%</td>
<td>29%</td>
</tr>
<tr>
<td>All HcT Tests Under 45%</td>
<td>22%</td>
</tr>
</tbody>
</table>

At least 1 HcT test received is above 50%
No HcT tests received are above 50%
Every HcT test a patient receives is below 45%

Symphony Patient Journey Data, August 2020
## Thrombotic Events in Treated PV Patients

**Patient data n=28,306**

- For patients with a prior thrombotic event, 40% had at least another one while on treatment
- For patients without prior thrombosis, 10% had at least one thrombotic event during treatment

### Risk Group

<table>
<thead>
<tr>
<th>Risk Group</th>
<th>Total Patient Count</th>
<th>Patient with TE Post Treatment Initiation*</th>
<th>% of TE</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>n</td>
<td>%</td>
</tr>
<tr>
<td><strong>Low Risk Patients</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age &lt; 60 and No Prior TE</td>
<td>8,373</td>
<td>629</td>
<td>8%</td>
</tr>
<tr>
<td><strong>High Risk Patients</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All High-Risk Patients</td>
<td>19,933</td>
<td>3,920</td>
<td>20%</td>
</tr>
<tr>
<td>Patients with No Prior TE</td>
<td>14,346</td>
<td>1,688</td>
<td>10%</td>
</tr>
<tr>
<td>Patients with Prior TE</td>
<td>5,587</td>
<td>2,232</td>
<td>40%</td>
</tr>
</tbody>
</table>

*Thrombotic events are evaluated from treatment initiation through Mar 2020. Median look-forward period is 808 days.*
Elevated HcT Resulted 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

Rufsertide Market Opportunity for PV

There are approximately 160,000 people in the United States living with PV\(^1\)

- \(\sim 100,000\) treated patients
- Growing market with \(\sim 14,000\) new patients diagnosed annually
- Median survival in PV approaches or can exceed 20 years

**Majority of diagnosed patients are treated**

- PV patients on average see their physician six times annually

**Large portion of the treated patient population appears to have sub-optimal control of HcT**

- Jakafi is the only product approved by the FDA in PV for hydroxyurea (HU) resistant/intolerant patients
- Besremi, a ropeginterferon alfa-2b product approved by the FDA with a Black Box warning in November 2021, is undergoing U.S. commercial launch with uncertain uptake at the present time.

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\(^1\) Mehta et al, Leuk. Lymphoma. 2014
\(^2\) Based on internal metrics and third-party research
HEPCIDIN

Natural Hormone and Master Regulator of Iron Homeostasis & Erythrocytosis

- Synthetically complex
  - 25-mer peptide with 4 interlinking disulfide bonds
  - High cost of goods (COGs)
- Stability, solubility, and aggregation challenges
  - Specialized formulations

RUSFERTIDE (PTG-300)

Hepcidin Mimetic: Investigational Therapy for Iron related Blood/Tissue Disorders

- Designed for superior drug-like properties
  - Potency (*in vitro*, *in vivo*), PK, solubility, stability (storage)
  - 18-mer peptide with 1 disulfide bond, easier synthesis, lower COGs
- Composition of matter US patents issued

Scaffold Hopping
De novo discovery
Hepcidin: Master Regulator of Iron Homeostasis

Rusfertide (PTG-300): Hepcidin Mimetic Designed to Bind and Internalize Ferroportin

1. Reduced iron release from macrophages
   - Iron sequestered in splenic macrophages is from recycled RBC

2. Reduce uptake of iron from diet
   - Inhibiting dietary iron export from enterocyte to circulation

Rusfertide: Mechanistic Rationale for Potential Treatment for PV

Reduces Excessive Red Blood Cell Production

Polycythemia Vera: Excessive RBCs

- Ferroportin (open)
- Low Hepcidin
- High Hematocrit 45

Rusfertide Reduces Erythrocytosis

- Ferroportin (closed)
- rusfertide Hepcidin-mimetic
- 45 Normal Hematocrit

Transferrin (TF)  Iron (Fe)  TF-FE  Erythroblast  JAK2  Red Blood Cell
Phase 2 Trial of Rusfertide in 63 PV Patients

GOAL: Maintain Hematocrit <45%

Add-On Study Design
Clinical GOAL: To maintain hematocrit <45%

<table>
<thead>
<tr>
<th>PART 1 (28 wks)</th>
<th>PART 2 (up to 12 wks)</th>
<th>PART 3 (52 wks)</th>
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<tbody>
<tr>
<td>Dose Finding*</td>
<td>Efficacy Evaluation*</td>
<td>Blinded Withdrawal</td>
</tr>
<tr>
<td>20 mg</td>
<td>40 mg</td>
<td>Fixed Active/Placebo Dose (1:1)</td>
</tr>
<tr>
<td>80 mg</td>
<td></td>
<td>Dose ± Titration</td>
</tr>
</tbody>
</table>

- *Titrate every 4 weeks to maintain hematocrit < 45%
- OLE increased from 52 weeks to 3 years
- First patient enrolled in Oct 2019, currently enrolling

ELIGIBILITY REQUIREMENTS:
- Phlebotomy dependent PV patients diagnosed as per 2016 WHO criteria
- ≥3 phlebotomies in 6 months with or without concurrent cytoreductive therapy
- All patients prior to first PTG-300 dose were phlebotomized to HCT < 45% to standardize the starting HCT
- PTG-300 doses of 10-120 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

In consultation with the U.S. Food and Drug Administration, Protagonist has implemented new safety monitoring procedures, including cancer surveillance measures (augmented dermatological examinations) and new stopping rules following a prior 21-day clinical hold on the rusfertide clinical development program. Re-enrollment continues with the target of 50 patients completing the full trial.
Overall, during the first 28 weeks of treatment, 84% of patients did not require a phlebotomy, 14% required one and 2% required two phlebotomies.
## Baseline Characteristics of Study Participants

### Characteristics (n = 63)

<table>
<thead>
<tr>
<th>Characteristics (n = 63)</th>
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<tbody>
<tr>
<td><strong>AGE</strong></td>
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<tr>
<td>Range</td>
<td>27-76 years (Mean = 56.3 yrs)</td>
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<tr>
<td><strong>GENDER</strong></td>
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<tr>
<td>Females</td>
<td>18 (28.8%)</td>
</tr>
<tr>
<td>Males</td>
<td>45 (71.4%)</td>
</tr>
<tr>
<td><strong>RISK</strong></td>
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<tr>
<td>Low</td>
<td>28 (44.4%)</td>
</tr>
<tr>
<td>High</td>
<td>35 (55.6%)</td>
</tr>
<tr>
<td>[Age based – 36.5%, Thrombotic events – 19.0%]</td>
<td></td>
</tr>
<tr>
<td><strong>DURATION SINCE PV DIAGNOSIS</strong></td>
<td></td>
</tr>
<tr>
<td>&lt;1 yr</td>
<td>12 (19.0%)</td>
</tr>
<tr>
<td>1 - &lt;3 yrs</td>
<td>23 (36.5%)</td>
</tr>
<tr>
<td>3 - &lt;5 yrs</td>
<td>9 (14.3%)</td>
</tr>
<tr>
<td>≥5 yrs</td>
<td>19 (30.2%)</td>
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### Characteristics (n = 63)

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<th>Characteristics (n = 63)</th>
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<tr>
<td><strong>THERAPIES</strong></td>
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<tr>
<td>PHL only</td>
<td>31 (49.2%)</td>
</tr>
<tr>
<td>PHL + HU</td>
<td>18 (28.6%)</td>
</tr>
<tr>
<td>PHL + IFN</td>
<td>8 (12.7%)</td>
</tr>
<tr>
<td>PHL + RUX</td>
<td>3 (4.8%)</td>
</tr>
<tr>
<td>PHL + Multiple Agents</td>
<td>3 (4.8%)</td>
</tr>
<tr>
<td><strong>NUMBER OF PHL IN 28 WEEKS PRIOR</strong></td>
<td></td>
</tr>
<tr>
<td>2-3</td>
<td>15 (23.8%)</td>
</tr>
<tr>
<td>4-5</td>
<td>33 (52.3%)</td>
</tr>
<tr>
<td>≥6</td>
<td>15 (23.8%)</td>
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<tr>
<td><strong>DAYS BETWEEN PHLEBOTOMIES</strong></td>
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<tr>
<td>Range</td>
<td>2-10 (Mean 4.71)</td>
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<tr>
<td>Median</td>
<td>35</td>
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</table>
Rusfertide Controls HCT and Reduces RBC Count

Rusfertide Controls HCT for 1.5 year

**Weeks**

- N = 63
- HCT (%) 33, 39, 45, 51
- Box whiskers extend up to 1.5 times interquartile range.

**Part 1 – Dose Finding**

**Part 2/3 – Blinded Withdrawal/OLE**

**Part 3 – Open Label Extension**

Rusfertide reduces RBC Count in PV patients

**Weeks**

- N = 63
- RBC (10^6/μL) 3, 4, 5, 6, 7
- Box whiskers extend up to 1.5 times interquartile range.

- **P<0.01**
- **AVAL = Raw Value**
- **Box whiskers extend up to 1.5 times interquartile range.**

Data as of September 2021
Rusfertide Normalizes Iron Stores

Data as of September 2021
Effects of Rusfertide on Platelet and WBC Counts

**Platelets**

- **Weeks:**
  - Screening
  - Part 1 – Dose Finding
  - Part 2 – Blinded Withdrawal
  - Part 3 – Open Label Extension

- **AVAL = Raw Value**
- **Box whiskers extend up to 1.5 times interquartile range.**

- **All increases in Platelet numbers < 20%**

**WBC**

- **Weeks:**
  - Screening
  - Part 1 – Dose Finding
  - Part 2 – Blinded Withdrawal
  - Part 3 – Open Label Extension

- **AVAL = Raw Value**
- **Box whiskers extend up to 1.5 times interquartile range.**

Data as of September 2021
Improvement in MPN-TSS Scores Following Rusfertide

### Total Symptom Score

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Week 8</th>
<th>Week 16</th>
<th>Week 24</th>
<th>Week 28</th>
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<tbody>
<tr>
<td>N</td>
<td>62</td>
<td>56</td>
<td>50</td>
<td>3</td>
<td>24</td>
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<tr>
<td>16.3</td>
<td>15.2</td>
<td>14.6</td>
<td>13.3</td>
<td>11.4</td>
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### Worst Level of Fatigue

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<th>Week 28</th>
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<tbody>
<tr>
<td>Paired Mean</td>
<td>3.2</td>
<td>2.7</td>
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### Problems with Concentration

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<th>Week 28</th>
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<tbody>
<tr>
<td>Paired Mean</td>
<td>1.9</td>
<td>0.9</td>
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### Itching-Pruritus

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<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Week 28</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paired Mean</td>
<td>2.3</td>
<td>1.6</td>
</tr>
</tbody>
</table>

Data as of September 2021

P = 0.04
Adverse Events Experienced on Rusfertide

<table>
<thead>
<tr>
<th>System Organ Class. - Preferred term</th>
<th>AE n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total number of Subjects</strong></td>
<td>63</td>
</tr>
<tr>
<td><strong>No. of subjects with treatment-emergent AE</strong></td>
<td>55 (87)</td>
</tr>
<tr>
<td>Blood and Lymphatic Disorders</td>
<td>12 (19.0)</td>
</tr>
<tr>
<td>Anemia</td>
<td>9 (14.3)</td>
</tr>
<tr>
<td>Gastrointestinal disorders</td>
<td>20 (31.7)</td>
</tr>
<tr>
<td>Nausea</td>
<td>8 (12.7)</td>
</tr>
<tr>
<td>Infections and infestations</td>
<td>11 (17.5)</td>
</tr>
<tr>
<td>Metabolism and nutrition disorders</td>
<td>9 (14.3)</td>
</tr>
<tr>
<td>Musculoskeletal and connective tissue disorders</td>
<td>27 (42.9)</td>
</tr>
<tr>
<td>Nervous system disorders</td>
<td>21 (33.3)</td>
</tr>
<tr>
<td>Psychiatric disorders</td>
<td>7 (11.1)</td>
</tr>
<tr>
<td>Insomnia</td>
<td>4 (6.3)</td>
</tr>
<tr>
<td>Renal and urinary disorders</td>
<td>5 (7.9)</td>
</tr>
<tr>
<td>Respiratory</td>
<td>14 (22.2)</td>
</tr>
<tr>
<td>Skin and subcutaneous tissue disorders</td>
<td>23 (36.5)</td>
</tr>
<tr>
<td>Pruritis</td>
<td>9 (14.3)</td>
</tr>
</tbody>
</table>

- Most Drug related AEs were Grade 1 or 2
- No Grade 4 or 5 Events
- SAE’s Syncope, peripheral artery aneurism, gastroenteritis, chest pain, AML, squamous cell carcinoma (skin), melanoma & basal cell carcinoma
- Injection site reaction (ISRs) were most common and associated with 28.1% of injections. All ISRs were transient, and no patient discontinued due to ISR.
- One subject stopped treatment due to AE within 2 weeks (asymptomatic thrombocytosis)
- No clinically significant laboratory abnormalities.
- No Anti Drug Antibody response was noted in any patient

Data as of September 2021
Rusfertide Phase 3 Study Design in PV

Enrollment Criteria, Primary Endpoint, Key Secondary Endpoints, Additional Assessments

**Enrollment Criteria:**
- Adult patients with PV per 2016 WHO Criteria
- High risk and low risk patients
- Patients requiring frequent phlebotomy
- With or without cytoreductive therapy
- Exclusion of patients with invasive cancer in prior 5 years

**Primary Endpoint:**
- Absence of phlebotomy eligibility based on hematocrit control between weeks 20-32

**Key Secondary Endpoints:**
- Frequency of phlebotomies
- Symptom improvement scores
- Safety

**Additional Assessments:**
- Durability of response weeks 32-52
- Open-label treatment to evaluate long-term effects and safety
Phase 3 Design as Presented at ASH 2021
Poster Presentation: Double-Blind Placebo Controlled Phase 3 Study

250 PV Patients to be randomized across 100 Global sites - Dosing Starts in Q1 2021

* Phlebotomy history for up to 52 weeks
High Hematocrit Study

- Patient met the WHO criteria for PV diagnosis;
- Baseline hematocrit (HCT) > 48%, and a history of ≥3 HCT values > 48% in the year prior to enrollment;
- High-risk and low-risk subjects treated with TP alone or with concurrent cytoreductive therapy were eligible;
- Rusfertide was added on to each subject’s current therapy;
- **Initial dose**: 40 mg SQ twice weekly;
- **Maintenance dose**: Once each subject’s HCT decreased (< 45%) for 2 consecutive visits, physicians’ choice to adjust dosing regimen to maintain HCT < 45%.

Full overview available at https://clinicaltrials.gov/ct2/show/NCT04767802
Baseline Characteristics of PV Subjects (n=20)

- **Age Group (y)**
  - <= 60: 65%
  - > 60: 35%

- **Risk Level**
  - High: 35%
  - Low: 65%

- **Gender**
  - Female: 25%
  - Male: 75%

- **PHL + HU**
  - 80%

- **Concurrent Therapy**
  - PHL Alone: 20%
  - PHL + HU: 80%

- **Phlebotomies in prior 28 Weeks**
  - 0: 35%
  - 1-2: 15%
  - 3-4: 15%
  - >=5: 30%

- **Duration since PV Diagnosis**
  - <1 yr: 20%
  - 1 to <3 yrs: 15%
  - 3 to <5 yrs: 15%
  - >=5 yrs: 30%

Data as of September 2021
High HCT Study: Therapeutic Phlebotomies Prior to and on Rusfertide

Data as of September 2021
Rusfertide Rapidly Controls HCT and Reduces RBC

**Rusfertide Immediately Controls HCT**

<table>
<thead>
<tr>
<th>Weeks</th>
<th>HCT (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prior</td>
<td>50.20</td>
</tr>
<tr>
<td>-24Wks</td>
<td>48.64</td>
</tr>
<tr>
<td>-16Wks</td>
<td>46.62</td>
</tr>
<tr>
<td>-8Wks</td>
<td>44.21</td>
</tr>
<tr>
<td>20</td>
<td>&gt;0.01</td>
</tr>
<tr>
<td>18</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>17</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>13</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>11</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>9</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>4</td>
<td>0.04</td>
</tr>
<tr>
<td>3</td>
<td>0.04</td>
</tr>
</tbody>
</table>

**P<0.01**

**Rusfertide Immediately Reduces RBC Count**

<table>
<thead>
<tr>
<th>Weeks</th>
<th>RBC (10^6/uL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>11.00</td>
</tr>
<tr>
<td>Wk 4</td>
<td>10.01</td>
</tr>
<tr>
<td>Wk 8</td>
<td>9.01</td>
</tr>
<tr>
<td>Wk 12</td>
<td>8.01</td>
</tr>
<tr>
<td>Wk 16</td>
<td>7.01</td>
</tr>
<tr>
<td>Wk 20</td>
<td>6.01</td>
</tr>
<tr>
<td>Wk 24</td>
<td>5.01</td>
</tr>
<tr>
<td>Wk 28</td>
<td>4.01</td>
</tr>
</tbody>
</table>

**P<0.01**

Data as of September 2021
Rusfertide Normalizes Iron Stores

Data as of September 2021

FERRITIN (ug/L)

P<0.01

Weeks

TSAT (fraction)

P=0.02   P=0.51

MCV (um3)

P<0.01

Screening  PTG-300  MEAN
Effects of Rusfertide on Platelet Count and WBC Count

PTG-300 Leads to Increased WBC count

PTG-300 Leads to Increased Platelet Count

Data as of September 2021
Platelets ($10^3$/uL) Over Time by Subjects

Data as of September 2021
Adverse Events in Ongoing Study PTG-300-08

- Most Drug related AEs were Grade 1 or 2
- One subject stopped treatment due to AE (Thrombocytosis without bleeding or thrombosis; Grade 4 according to investigator)
- Injection site reaction (ISRs) were most common and associated with 68% of injections. All ISRs were transient, and no patient discontinued due to ISR.
- No anti-drug antibody response was noted in any patient

<table>
<thead>
<tr>
<th>System Organ Class</th>
<th>Preferred term</th>
<th>All AEs n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total number of Subjects</td>
<td></td>
<td>20</td>
</tr>
<tr>
<td>No. of subjects with treatment-emergent AE</td>
<td></td>
<td>13 (65.0)</td>
</tr>
<tr>
<td>Blood and Lymphatic System</td>
<td></td>
<td>3 (15.0)</td>
</tr>
<tr>
<td>Thrombocytosis</td>
<td></td>
<td>3 (15.0)</td>
</tr>
<tr>
<td>Gastrointestinal disorders</td>
<td></td>
<td>3 (15.0)</td>
</tr>
<tr>
<td>Nausea</td>
<td></td>
<td>5 (8.1)</td>
</tr>
<tr>
<td>Musculoskeletal and connective tissue disorders</td>
<td></td>
<td>3 (15.0)</td>
</tr>
<tr>
<td>Nervous system disorders</td>
<td></td>
<td>5 (25.0)</td>
</tr>
<tr>
<td>Renal and urinary disorders</td>
<td></td>
<td>2 (3.2)</td>
</tr>
<tr>
<td>Skin and subcutaneous tissue disorders</td>
<td></td>
<td>4 (20.0)</td>
</tr>
</tbody>
</table>
Conclusions: High Hematocrit Study

- PTG-300 (Rusfertide) induction therapy with twice weekly dosing is effective at rapidly achieving target hematocrit below 45% without phlebotomy in all erythrocytotic PV patients.

- PV patients initially on twice weekly injections of rusfertide rapidly lower hematocrit levels enabling successful transition to and maintenance on weekly Rusfertide treatment.

- The clinical significance of increased platelet and WBC counts (in the absence of a thrombotic event) in a subset of PV patients on rusferitide remains to be fully evaluated with longer follow up of a larger cohort of PV patients.

Taken together, use of rusfertide in erythrocytotic PV patients represents a novel therapeutic direction for patients unwilling or unable to utilize the current standard of care.
Rufsertide Market Preparation: PV Indication

Intend to Demonstrate Clinical & Economic Value Before Approval

Value Proposition
- Patients
- Prescribers
- Payers

Distribution Channels
Patient access

Market Access
Pricing & Reimbursement Strategy

HEOR
Health Economics & Outcomes Research for assessing economic burden and benefit of treatment

Prescriber Education
Raise awareness of PV, unmet need and NCCN Guidelines

Competitive Landscape
Existing and future treatments

Positioning Strategy
Leader in the treatment of PV
Hereditary Hemochromatosis (HH)

**Disease Prevalence and Treatment**

- **Iron overload disease**
- **Unmet medical need in specific subpopulations**
- **Phlebotomy is the only therapeutic option; no approved drugs**
- **Excessive iron accumulation in heart, liver, pancreas, skin, joint tissues**

**If untreated, iron overload can cause**
hepatomegaly, diabetes mellitus, skin hyperpigmentation, cardiomyopathy, diastolic dysfunction, heart failure, cirrhosis, etc.

Hereditary Hemochromatosis (HH)

Overview: Rusfertide (PTG-300) Rationale and Phase 2 Clinical PoC Study Design

Rusfertide (PTG-300) rationale

• HH is predominately due to genetic mutation, leading to a deficiency of hepcidin in the body
• Rusfertide, if approved, could serve as a hormone replacement therapy

Ph2 Clinical PoC Study

• 16 patient open-label study
• Efficacy measures
  1. PD readouts: serum Iron, TSAT, ferritin
  2. Phlebotomy reduction
  3. Organ liver load: Liver iron concentration (LIC) by MRI
  4. Quality of Life (QOL) effects: SF-36, PGI-C

Clinical ‘Proof of Concept’ Study Design

- N=16
- 10 mg, 20 mg, 40 mg dosed once or twice a week
- Adjust dose to maintain TSAT <40%

Screen (Scrn) to Wk 0
- Wk 24
### Detailed Phase 2 Proof of Concept Study Design: HH

**Dose adjustment to maintain serum iron and TSAT < 40%**

<table>
<thead>
<tr>
<th></th>
<th>Screening</th>
<th>Month 1</th>
<th>Month 2</th>
<th>Month 3</th>
<th>Month 4</th>
<th>Month 5</th>
<th>Month 6</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Dosing</strong></td>
<td>-</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Assessments</strong></td>
<td>-</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Phlebotomy</strong></td>
<td>Within 7 days prior to dosing</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Liver MRI</strong></td>
<td>Within 7 days prior to dosing</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Endpoints</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Dosing:** Subcutaneous, self-administered once or twice weekly. Dose adjusted based on TSAT and serum iron

**Assessments:** Adverse Events, PK, PD (iron parameters – TSAT, serum iron, ferritin, transferrin)

**Phlebotomy:** As required on study. Criteria were serum ferritin levels and TSAT values higher than the pre-phlebotomy values at Screening or if Investigator deemed necessary for subject care

**Liver MRI:** At end of 6-month study treatment

**Endpoints:** Safety, Reduction in phlebotomies, Serum iron, TSAT, transferrin, ferritin, Liver Iron Content by MRI
# Phase 2 Proof of Concept Study: HH

## Inclusion and Exclusion Criteria

### Inclusion

- Adults with diagnosis of *HFE*-related hereditary hemochromatosis with prior genotype testing
- Documented stable phlebotomy for ≥6 months prior to screening; received at least three phlebotomies over the previous 12 months, or at least four phlebotomies over the previous 15 months and not more than 1 per month
- Screening Hb >11.5 g/dL
- Serum ferritin <300 ng/mL at screening

### Exclusion

- Laboratory values
  - Absolute neutrophil count <1000/μL
  - Platelet count <100,000/μL
  - Estimated Glomerular Filtration Rate (eGFR) <40 mL/min/1.73 m²
  - Alanine aminotransferase (ALT) or aspartate aminotransferase (AST) ≥2.5 × upper limit of normal (ULN) or direct bilirubin >1.5 × ULN
  - C-reactive protein (CRP) ≥5.0 mg/L
- Receiving iron chelation therapy
- Receiving erythrocytapheresis
- Evidence of end-organ damage
### Phase 2 Proof of Concept Study: HH

#### Baseline Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y (range)</td>
<td>62.5±12.3 (31.0-77.0)</td>
</tr>
<tr>
<td>Age ≥ 65 y (%)</td>
<td>6 (37.5%)</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>10 (62.5%)</td>
</tr>
<tr>
<td>No of Phlebotomies in 24 weeks (range)</td>
<td>2.31±1.0 (1-4)</td>
</tr>
<tr>
<td>3-4</td>
<td>7 (43.8%)</td>
</tr>
<tr>
<td>1-2</td>
<td>9 (56.3%)</td>
</tr>
<tr>
<td>Serum Iron, mcg/dL (range)</td>
<td>137±60 (39-241)</td>
</tr>
<tr>
<td>TSAT, % (range)</td>
<td>43.1±23.7 (10-80)</td>
</tr>
<tr>
<td>Serum Ferritin, mcg/L (range)</td>
<td>82.3±57.6 (11.2-190.4)</td>
</tr>
<tr>
<td>Serum Transferrin, g/L (range)</td>
<td>2.3±0.4 (1.8, 3.1)</td>
</tr>
</tbody>
</table>
Rusfertide Reduced Phlebotomy Utilization in Most Subjects

Data as of September 2021
Effect of Rusfertide on Serum Iron and TSAT

Data as of September 2021
Effect of Rusfertide on Serum Iron and TSAT

Data as of September 2021
Effect of Rusfertide on Transferrin and Ferritin

Data as of September 2021

- Transferrin (mg/dL)
  - Baseline
  - Average Post Rusfertide
  - 0.0006

- Ferritin (μg/L)
  - Baseline
  - Average Post Rusfertide
  - 0.3893
Rusfertide Was Associated with Reduced Liver Iron Content

- Subjects were in maintenance phase and on phlebotomy pre-study, and LIC levels were not elevated
  - Pre-study: 1.8 mg/g dry tissue
  - Post-study: 0.9 mg/g dry tissue
- Expectation is that rusfertide would maintain LIC levels in the absence of phlebotomy

Data as of September 2021
### Adverse Events Reported in ≥2 subjects

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No of Subject with At least one Treatment-Emergent AE</td>
<td>13 (81.3%)</td>
</tr>
<tr>
<td>No of Subject with Serious Adverse Events</td>
<td>1 (6.3%)a</td>
</tr>
<tr>
<td><strong>Gastrointestinal Disorders</strong></td>
<td></td>
</tr>
<tr>
<td>Diarrhea</td>
<td>2 (12.5%)</td>
</tr>
<tr>
<td><strong>General and Administration Site Conditions</strong></td>
<td></td>
</tr>
<tr>
<td>Injection site pain</td>
<td>5 (31.3%)</td>
</tr>
<tr>
<td>Injection site erythema</td>
<td>2 (12.5%)</td>
</tr>
<tr>
<td>Injection site induration</td>
<td>2 (12.5%)</td>
</tr>
<tr>
<td>Injection site pruritis</td>
<td>2 (12.5%)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>2 (12.5%)</td>
</tr>
<tr>
<td><strong>Nervous System Disorders</strong></td>
<td></td>
</tr>
<tr>
<td>Dizziness</td>
<td>2 (12.5%)</td>
</tr>
<tr>
<td>Headache</td>
<td>2 (12.5%)</td>
</tr>
<tr>
<td><strong>Vascular Disorders</strong></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>2 (12.5%)</td>
</tr>
</tbody>
</table>

- All AEs were Grade 1 or 2
- No adverse events of anemia

*a* Adenocarcinoma of the pancreas considered a pre-existing condition not related to drug.

Data as of September 2021
Rusfertide, a hepcidin mimetic:
• significantly reduced the number of phlebotomies,
• lowered serum iron and TSAT
• liver iron content were reduced
• was generally well tolerated

Additional studies are required to further characterize the safety, efficacy, and long-term outcomes in HH
Hereditary Hemochromatosis (HH)

Identifying Patients with Highest Unmet Need

Market assessment is underway across multiple dimensions of the patient experience

- Frequency of phlebotomy
- Phlebotomy “ineligible” sub-populations
- Severity of symptoms
- Comorbidities
- Concomitant therapies
- Rate and patterns of disease progression, including progression to liver damage and failure

Severity of unmet need will guide our strategy as we continue to collect and evaluate data
PN-943 and IL-23 Receptor Antagonists
Oral Targeted Investigational Therapies for IBD and non-IBD indications
IBD: Paradigm Shift Toward Targeted Oral and Combination Therapy

A Growing Multi-Billion Dollar Market

2019: ~ $14B sales¹

Historical IBD Treatment Paradigm

**TNF mAbs dominated IBD Therapy**
- Injectable TNF mAbs – Blockbusters
  - Humira® & Remicade®
- Significant room for improvement
  - Low response rates / loss of response
  - Safety concerns - black box warnings

2029: projected ~ $24B sales¹

Emerging IBD Treatment Paradigm

**Injectable mAbs with safer MOAs**
- α4β7 integrin: Entyvio® (~ $4B sales 2020)
- IL-12/IL-23: Stelara®

**Oral Targeted Therapy for IBD**
Protagonist: **mAb Validated Pathways**
- PN-943 (α4β7 integrin)
- IL-23Rs

**Other Oral Approaches: New Targets**
- S1P1: ozanimod, etrasimod
- JAK*: Xeljanz®, Rinvoq®, filgotinib
* black box warnings

Potential Future of IBD Oral Combo Therapy

1 GlobalData: Global Drug Forecast and Market Analysis to 2029; 7 Major Markets: US, EU5, JP
2 Investigational product candidate, not approved
Oral, Gut-Restricted, α4β7-Integrin Peptide Antagonists: PN-943

Fully Owned and Validated Asset and Approach

Clinically Validated, IBD Specific Target

- T cell homing regulated by α4β7 integrin and MAdCAM-1 interaction
- MAdCAM-1 expressed only in GI vasculature
- Entyvio (Vedolizumab) approved for Crohn’s & UC
  - ~$4B fiscal 2020 sales
- Superior efficacy for Entyvio vs. Humira in 52 wk Ph3B VARSITY study

PN-943: Validated, Gut-restricted Approach

- First-in-class potential as an oral, GI-restricted α4β7-specific antagonist
- PN-943 is ~3x more potent in numerous pre-clinical studies & Ph1 NHV study vs 1st generation candidate PTG-100 (DDW, 2019)¹
  - PTG-100 showed signals of clinical efficacy in Ph2a UC trial (UEGW, 2018)²
- PN-943 global Ph2 150 patient study in UC patients in progress
- Study completion anticipated in 2Q 2022*
Clinical Validation From PTG-100

Phase 2a Histologic and Clinical Remission

<table>
<thead>
<tr>
<th>Clinical Readout</th>
<th>Clinical Study</th>
<th>Placebo</th>
<th>900 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical Remission*</td>
<td>Ph 2a UC</td>
<td>4.8% (1/21)</td>
<td>15.8% (3/19)</td>
</tr>
<tr>
<td>Histologic Remission**</td>
<td>Ph 2a UC</td>
<td>0% (0/13)</td>
<td>44% (7/16)</td>
</tr>
</tbody>
</table>

*Clinical remission defined as Mayo rectal bleeding score of 0, endoscopic subscore of 0/1, and a stool frequency score of 0/1 with at least a 1-point reduction from baseline

**Histologic remission defined as a Week 12 RHI score of ≤ 3 amongst patients who had a score > 3 at baseline

- Dose-related, most efficacious at **900 mg** QD dose in UC patients at 12 weeks
  - 11% delta over PBO similar to clinical remission rates for most other IBD targeted drugs
- High rate and dose dependent histologic remission
  - 44% at 900 mg dose
- PTG-100 is safe and well-tolerated
PN-943: First-in-Class Oral $\alpha 4\beta 7$ Integrin Antagonist

PN-943 superior to first generation PTG-100
- In vitro potency and binding kinetics
- Blood PD effects of local target engagement in 3 species
- Efficacy in rodent colitis model
- Similar selectivity, oral stability and limited blood exposure

PN-943 was advanced into clinical development in 2019
- Based on preclinical superiority over PTG-100
- Oral approach validated by PTG-100 PROPEL Ph2a data

Future Potential
- MEDACorp IBD Physician Survey: “oral anti-integrins were found to be the most exciting unapproved drug class in UC”
- Anchor for combination therapy in the paradigm shift of IBD treatment

<table>
<thead>
<tr>
<th>Integrin</th>
<th>$\alpha 4\beta 7$ (IC$_{50}$ nM)</th>
<th>$\alpha 4\beta 1$ (IC$_{50}$ nM)</th>
<th>$\alpha L\beta 2$ (IC$_{50}$ nM)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adhesion Ligand</td>
<td>MAdCAM-1</td>
<td>VCAM-1</td>
<td>ICAM-1</td>
</tr>
<tr>
<td>PN-943</td>
<td>0.27</td>
<td>&gt; 12,000</td>
<td>&gt; 50,000</td>
</tr>
</tbody>
</table>
PN-943 vs. PTG-100: Blood %RO based Clinical Proof-of-Concept
Ph1 NHV Single Ascending Dose Study

PTG-100 Ph2 UC PoC

<table>
<thead>
<tr>
<th>Ph2A Study UC</th>
<th>PTG-100 900 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Histologic Remission</td>
<td>44% (7/16)</td>
</tr>
<tr>
<td>Clinical Remission*</td>
<td>16% (3/19)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Ph 1 Study NHVs</th>
<th>PTG-100 1000 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>% Blood RO</td>
<td>74%</td>
</tr>
</tbody>
</table>

*Based on blinded endoscopic re-reads
*Clinical remission: SFS ≤1, RBS = 0, ESS ≤1

Established 74% blood RO in healthy subjects as a translational benchmark

PN-943 vs PTG-100 Ph1 Data

**Ph1 SAD**

- 100 mg: 83% ± 4%
- 300 mg: 74% ± 4%
- 1000 mg: 94% ± 4%

**Ph1 MAD, Day 14**

- 100 mg: 80% ± 4%
- 300 mg: 74% ± 4%
- 1000 mg: 96% ± 4%

PN-943 vs. PTG-100 Ph1 NHV study

- Higher effect on blood %RO confirms ~3x superiority of PN-943 vs. PTG-100
  - PN-943 300mg blood %RO > PTG-100 1000 mg blood %RO effect
- Saturable target engagement at 1000 mg QD dose

PTG-100 Ph2A Efficacy Similar to Other IBD Targeted Therapy Drugs

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Patients in Clinical Remission</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tofacitinib</td>
<td>905 17.6 11.6 6 6.2 9 11.6 6</td>
</tr>
<tr>
<td>Ozanimod</td>
<td>234 15.2 6.2 6.2 9 11.6 6.2 9</td>
</tr>
<tr>
<td>Etrolizumab</td>
<td>132 15.3 0 2.7 2.7 2.7 2.7 2.7</td>
</tr>
<tr>
<td>SHF-647*</td>
<td>81  15.3 9.6 2.7 2.7 2.7 2.7 2.7</td>
</tr>
<tr>
<td>Entyvio</td>
<td>284 12.3 9.6 2.7 2.7 2.7 2.7 2.7</td>
</tr>
<tr>
<td>PTG-100 900 mg q.d.</td>
<td>225 16.9 11.5 5.4 5.4 5.4 5.4 5.4</td>
</tr>
<tr>
<td>Placebo</td>
<td>73   15.8 11.5 4.8 4.8 4.8 4.8 4.8</td>
</tr>
<tr>
<td>Delta</td>
<td>225  149 19 149 19 149 19 149</td>
</tr>
</tbody>
</table>

*Anti-MadCam mAb
* No central read endoscopy (Entyvio)
Thirty subjects received multiple doses with 68 total AEs

Treatment-emergent adverse events reported in 2 or more subjects included abdominal discomfort, flatulence, upper respiratory tract infection, back pain, dizziness, and headache

Four subjects receiving placebo reported a total of 6 mild TEAEs, primarily gastrointestinal disorders

No clinically relevant changes were observed in respiratory rate, vital signs, clinical laboratory parameters, and electrocardiograms
Adult Patients with UC
N=150

Eligibility:
- Moderate – Severe UC
- 3-Component Mayo Score 5-9 points

Inclusion:
- Bio-naïve and bio-experienced patients

Primary endpoint:
- Clinical Remission at Week 12

Extended drug treatment:
- Active drug for 40 weeks after 12-week induction phase completion

Part-1: Induction
- Randomize (n=150)
  - Placebo BID (n=50)
  - Active Drug 150 mg BID (n=50)
  - Active Drug 450 mg BID (n=50)

Part-2: Extended Treatment Period
- PN-943
- 40 Weeks
- Week 52

Study completion and preliminary data readout anticipated in Q2 2022*
Oral, IL-23 Receptor Specific Peptide Antagonist: PN-235

Janssen Partnership

Objective
- Extend the Stelara® franchise and transition from injectable to oral targeted therapy
  - Stelara approved for psoriasis, psoriatic arthritis, Crohn’s, UC

Terms
- May 2017: Partnership initiated
- $87.5M in upfront and development milestones received to date
- Eligible for about additional $900M in milestones, up to double digit royalties, US co-detailing rights
- Amendments in 2019 and 2021

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 in progress; completion in 2021; advancing in psoriasis indication in early 2022 and in IBD indications in 2H 2022

Stelara® is a key Janssen franchise
- ~$7.7B total global sales in 2020
PROTAGONIST THERAPEUTICS
Protagonist Team and Financials
<table>
<thead>
<tr>
<th>Name</th>
<th>Title</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dinesh Patel, PhD</td>
<td>President &amp; CEO</td>
</tr>
<tr>
<td>David Liu, PhD</td>
<td>CSO, Head of Discovery &amp; Pre-Clinical Dev</td>
</tr>
<tr>
<td>Samuel Saks, MD</td>
<td>Clinical Development Advisor</td>
</tr>
<tr>
<td>Suneel Gupta, PhD</td>
<td>Chief Development Officer</td>
</tr>
<tr>
<td>Donald Kalkofen</td>
<td>Chief Financial Officer</td>
</tr>
<tr>
<td>Tracy Woody</td>
<td>EVP, Commercial Strategy</td>
</tr>
<tr>
<td>Matthew Gosling</td>
<td>EVP, General Counsel</td>
</tr>
<tr>
<td>Mohammad Masjedizadeh, PhD</td>
<td>EVP, Chief Technical Officer</td>
</tr>
<tr>
<td>Scott Plevy, MD</td>
<td>EVP &amp; Therapeutic Head, Gastroenterology</td>
</tr>
<tr>
<td>Ashok Bhandari, PhD</td>
<td>SVP, Discovery Chem &amp; Process Res</td>
</tr>
<tr>
<td>Paula O' Connor, MD</td>
<td>SVP, Clinical Development</td>
</tr>
<tr>
<td>Abha Bommireddi, MS</td>
<td>SVP, Program Management</td>
</tr>
<tr>
<td>Carter King</td>
<td>SVP, Business Development</td>
</tr>
<tr>
<td>Nishit Modi, PhD</td>
<td>SVP, Clinical Pharmacology</td>
</tr>
<tr>
<td>Sarita Khanna, PhD</td>
<td>SVP, Biometrics</td>
</tr>
</tbody>
</table>
Financial Highlights

Financial resources forecast extends through full year 2024

<table>
<thead>
<tr>
<th>CASH &amp; SECURITIES</th>
<th>2024</th>
<th>GROSS PROCEEDS</th>
<th>SHARES OUTSTANDING</th>
</tr>
</thead>
<tbody>
<tr>
<td>As of September 30, 2021</td>
<td>$352.5M</td>
<td>Raised in June 2021 offering: 3.5m shares issued at $37.75 per share, including 15% underwriter option exercised</td>
<td>As of September 30, 2021</td>
</tr>
<tr>
<td>CASH &amp; SECURITIES provide financial resources forecast through full year 2024</td>
<td></td>
<td>$132.2M</td>
<td>47.7M</td>
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</tbody>
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$352.5M
2024
$132.2M
47.7M
### Anticipated Timeline

#### 2021
- **Rusfertide Ph2 PV trial update at medical conferences**
  - EHA 2021 ☑ & ASH 2021 ☑
- **Ph2 POC data for rusfertide in HH ☑**
  - AASLD 2021 ☑ & ASH 2021 ☑
- **Completed PN-235 Ph1 study ☑**
- **PN-235 selected for psoriasis & IBD ☑**

#### 2022
- **Initiate rusfertide Ph3 trial in PV**
- **Ph2 completion and topline results for PN-943**
- **PN-235 Ph2 study initiation in psoriasis, $25m milestone to be earned**
- **PN-235 study initiation in one or more IBD indications in 2H 2022, qualifying for a $10m milestone payment**
- **New discovery targets & development candidates**

### Anticipated Key Event

<table>
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<th>Anticipated Key Event</th>
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| 2021                 | **Rusfertide Ph2 PV trial update at medical conferences**
|                      | EHA 2021 ✔ & ASH 2021 ✔
|                      | Ph2 POC data for rusfertide in HH ✔
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| 2022                 | **Initiate rusfertide Ph3 trial in PV**
|                      | Ph2 completion and topline results for PN-943
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|                      | PN-235 study initiation in one or more IBD indications in 2H 2022, qualifying for a $10m milestone payment
|                      | New discovery targets & development candidates

### Growth Advantages: Three Major Pillars

- **Rusfertide and PN-943**
  - Two fully owned product candidates in Phase 2
- **IL-23R Janssen Collaboration**
  - PN-235 advancing in multiple indications, including psoriasis and IBD
- **Innovative Technology Platform**
  - New discovery programs with potential to generate new assets
THANK YOU