COMPANY OVERVIEW

Dinesh V. Patel, PhD
President & CEO

June 2020
Forward Looking Statements

This presentation contains forward-looking statements of Protagonist Therapeutics, Inc. (Protagonist) that involve substantial risks and uncertainties. All statements other than statements of historical facts contained in this presentation, including statements regarding our future results of operations and financial position, our capital resources, business strategy, prospective products, potential market for our products, availability of funding, enrollment in our clinical trials, clinical trial results, product approvals and regulatory pathways, timing and likelihood of success, plans, objectives and opinions of management regarding future operations, future results of current and anticipated products and our potential receipt of milestone payments and royalties under our Exclusive License and 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.

We have based these forward-looking statements largely on our current expectations and projections about future events and trends that we believe may affect our financial condition, results of operations, business strategy and financial needs. These statements 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 risk and uncertainties include, among other things the success, cost and timing of our product development activities and clinical trials; our expectations about the timing of achieving regulatory approval and the cost of our development programs; our ability to obtain funding for our operations, including funding necessary to complete further development and commercialization of product candidates; the commercialization of our product candidates, if approved; our plans to research, develop and commercialize our product candidates; our ability to attract collaborators with development, regulatory and commercialization expertise; our expectations regarding our ability to obtain and maintain intellectual property protection for our product candidates; future agreements with third parties in connection with the commercialization of our product candidates; our ability to maintain, expand, protect and enforce our intellectual property portfolio; our ability to operate our business without infringing, misappropriating or otherwise violating the intellectual property rights of third parties; the size and growth potential of the markets for our product candidates, and our ability to serve those markets; the rate and degree of market acceptance of our product candidates; regulatory developments in the United States and foreign countries; our ability to contract with third-party suppliers and manufacturers and their ability to perform adequately; the success of competing therapies that are or may become available; and our ability to attract and retain key scientific or management personnel. Protagonist discusses many of these risks and uncertainties in detail under the heading “Risk Factors” contained in our most recent periodic reports on Forms 10-K and 10-Q, which are filed with the Securities and Exchange Commission. These risks are not exhaustive. New risk factors emerge from time to time and it is not possible for our management to predict all risk factors, nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in, or implied by, any forward-looking statements. 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 undertake no obligation to publicly update or revise any forward-looking statements contained herein after the date of this presentation, 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 (FDA). 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: Peptide Based Innovative Medicine

Three Assets in Clinical Proof-of-Concept Studies

1. Three clinical assets
   - De novo discovery using peptide technology platform
   - Multi billion-dollar portfolio potential

2. Clinical PoC studies in four different diseases
   - **PTG-300**: PV selected as the 1st indication for pivotal study; orphan drug designation (ODD) granted
   - **PTG-200**: partnered with Janssen; Ph2 Crohn’s study ongoing
   - **PN-943**: Ph2 UC study ready for initiation; COVID-19 related delay

3. Well financed through mid-2023
   - End of Q1 2020 ~ $117M
   - Net proceeds from capital raise in May ~$122.8M
PTG-300: HEPCIDIN MIMETIC
Address Unmet Needs in Rare Diseases
Hepcidin: Master Regulator of Iron Homeostasis

PTG-300 Hepcidin Mimetic Designed to Bind and Internalize Ferroportin

1. Reduce uptake of iron from diet
   - Inhibiting iron export from enterocyte to circulation mimics natural hepcidin’s regulation of iron

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

Hepcidin Mimetic PTG-300
Designed for Superior Drug-like Properties vs. Hepcidin

**Hepcidin**

- Natural Hormone and Master Regulator of Iron Homeostasis & Erythropoiesis
- Synthetically complex
  - 25-mer peptide with 4 interlinking disulfide bonds
  - High cost of goods (COGs)
- Stability, solubility, and aggregation challenges
  - Specialized formulations

**PTG-300**

- Hepcidin Mimetic: Investigational Therapy for Iron related Blood Disorders
- Designed for superior drug-like properties
  - Potency (*in vitro, in vivo*), PK, solubility, stability (storage)
  - Lower COGs, easier synthesis: 18-mer peptide with 1 disulfide bond
- Composition of matter US patents issued

**Vectrix™ Scaffold Hopping**

*De novo* discovery
PTG-300: A Single Product Portfolio
Polycythemia Vera, Hereditary Hemochromatosis

- Iron overload
- ~12 patient Ph2 POC study initiated
  - Study in progress; COVID-19 related delay in enrollment

Objective serum endpoints
- TSAT, Serum Fe
- Ferritin
- Hematocrit

• Ph2 Clinical POC ongoing
  - Small & preliminary data set but consistent trends
    - Hematocrit control
    - Phlebotomy free
PTG-300 Polycythemia Vera Ph2 Trial
PTG-300: A Non-Cytoreductive Hepcidin Hormone Mimetic
Polycythemia Vera Selected as First Indication for Pivotal Study

1. Preliminary data
   - Small data set but robust and consistent clinical responses
   - All dose compliant patients (6 out of 6) are phlebotomy free during 4-28 weeks of treatment (reported on May 7th)

2. Regulatory drug development path forward
   - Rare disease
   - Orphan drug designation (ODD) granted by US FDA (June 12th)

3. Commercial Opportunity
   - Significant unmet need; lack of new non-cytoreductive agents in development

Potential for First-in-class, Non-cytoreductive, Natural hormone Hepcidin mimetic based Therapy
Polycythemia Vera
Disease, Symptoms, Diagnosis, and Treatment

• Disease & Symptoms:
  – Myeloproliferative neoplasm characterized by an abnormal increase in red blood cells
  – Thrombotic events are the greatest risk to PV patients
  – Burdensome symptoms- fatigue, headache, visual disturbances, night sweats, itchiness

• Diagnosis:
  – Almost uniformly (>95%) characterized by a JAK2 mutation
  – Elevated hematocrit (>45%) is a hallmark of the disease

• Treatment: Goal is to control hematocrit <45%
  – Significant evidence showing that controlling hematocrit level below 45% is critical to minimizing thrombosis, CV events, and mortality
  – Phlebotomy is the most common and first treatment in newly diagnosed PV patients
    ▪ Not for everybody – inconvenience, anxiety, intolerance
    ▪ Exacerbates iron deficiency contributing to several non-hematological symptoms
    ▪ Hematocrit levels fluctuate between phlebotomy treatments, thereby posing CV risks
  – Cytoreductive therapies such as hydroxyurea (HU) used in combination with phlebotomy
    ▪ Jakafi is the only FDA approved product for PV
PTG-300: A Non-Cytoreductive Hepcidin Hormone Mimetic

Proposed Mechanism of Action for Potential Treatment of Polycythemia Vera

- Hepcidin hormone has an established role in promoting the sequestration of iron in macrophages, thereby decreasing iron availability for production of red blood cells (RBCs)

- PTG-300 potentially limits excess production of RBCs in PV limiting iron availability in bone marrow, and without causing systemic iron deficiency. As a result PTG-300 may potentially
  - Control erythrocytosis and hematocrit levels, thereby reducing thrombotic risk/events
  - Control symptoms of systemic iron deficiency such as those seen with PV and frequent phlebotomy
PV Prevalence and Treatment Regimens
Commercial Opportunity

- ~100,000 people in the U.S. living with PV and 98,000 in the EU5
- ~85% patients treated with phlebotomy or HU or combination
- Jakafi: only approved product in PV indicated for HU intolerant/resistant patients (~5,000)
  - PV sales were ~$625M in 2019 and is the fastest growing indication in Jakafi

1. Mehta et al, 2014 (US) and Orphanet 2019 (EU) 2. Grunwald 2018, REVEAL, n = 2510 patients
PTG-300 Phase 2 Study in Polycythemia Vera Patients
Clinical Proof-of-Concept Study Design

**GOAL: Maintain hematocrit ≤45%**

<table>
<thead>
<tr>
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<tbody>
<tr>
<td>Clinically Effective Dose Finding Phase*</td>
<td>Efficacy Evaluation Phase*</td>
<td>Randomized Withdrawal Phase</td>
</tr>
<tr>
<td>4 to 16 weeks</td>
<td>12 to 24 weeks</td>
<td>Up to 12 weeks</td>
</tr>
<tr>
<td>20 mg, 40 mg, 80 mg</td>
<td>Dose ± Titration</td>
<td>Fixed Active/Placebo Dose</td>
</tr>
<tr>
<td>4 to 16 weeks</td>
<td>12 to 24 weeks</td>
<td>Up to 12 weeks</td>
</tr>
<tr>
<td>20 mg, 40 mg, 80 mg</td>
<td>Dose ± Titration</td>
<td>Up to 52 weeks</td>
</tr>
</tbody>
</table>

*Titrate every 4 weeks to maintain hematocrit ≤ 45%*

- Safety, dose finding and efficacy evaluation study
- Three components – dose finding & efficacy evaluation, randomized withdrawal (~1:1), OLE
- Inclusion criteria: ≥3 phlebotomies in past 6 months; continue current therapy at stable doses
- Key endpoints
  - Safety
  - Maintain hematocrit <45%; reduction in phlebotomies
  - Symptom scores: change in MPN-SAF TSS
PTG-300 Controlled Hematocrit Below 45% in 6/7 Patients

Hematocrit (%)

-5 0 5 10 15 20 25
Weeks

45%
PTG-300 Restored Ferritin to Normal Range
Rescued From Iron Deficiency
Summary

PTG-300

PTG-300: Potential for First-in-class, Non-cytoreductive, Natural hormone Mimetic based Therapy for Polycythemia Vera

• Preliminary data in small number of patients is encouraging and demonstrates
  – Consistent hematocrit control <45% with once weekly administration without the up and down excursions inherent in typical phlebotomy therapy
    ▪ Hematocrit levels above 45% are associated with significant cardiovascular events
  – Potential to reduce or almost entirely avoid the need for phlebotomy
  – Potential to bring ferritin levels to normal levels thereby allowing sufficient iron to be available systemically and potentially avoid symptoms related to iron deficiency

• PTG-300 appears to be safe and well-tolerated

• Next Steps:
  – Expansion of current Ph2 study
  – Updates at major medical conferences
  – Planning and preparedness for pivotal study in 2021
Hereditary Hemochromatosis
Hereditary Hemochromatosis (HH)
Disease Overview and PTG-300 Rationale

Disease, Prevalence & Treatment

• Fairly common blood disorder
  – ~1.3M diagnosed patients in USA/Canada
  – causes the body to absorb too much iron from the diet, resulting in the accumulation of iron in tissues and organs, particularly in skin, heart, liver, pancreas and joint tissues
  – Confirm diagnosis with HFE, C282Y, and H63D mutations
  – Current treatment focuses on reducing iron through phlebotomy

• If untreated, iron overload can cause
  – Hepatomegaly, diabetes mellitus, skin hyperpigmentation, cardiomyopathy, diastolic dysfunction, heart failure, cirrhosis, etc

• HH treatment focuses on controlling serum transferrin saturation (TSAT) and ferritin levels to prevent long-term complications
  – Current treatment is phlebotomy; no approved drugs

PTG-300 Rationale

• HH is a genetic disorder predominantly due to a mutation in the HFE gene leading to a deficiency of hepcidin in the body.
  – PTG-300 could potentially serve as a hormone replacement therapy
• PTG-300 has shown significant TSAT reductions in both healthy volunteers and beta-thalassemia patients
• LJPC-401 (Hepcidin) showed positive results in Ph2 study
PTG-300 Ph2 Study in Hereditary Hemochromatosis Patients

Clinical ‘Proof of Concept’ Study Design

- ~12 patient POC study
  - Study in progress; COVID-19 related delay in enrollment
- Efficacy measures
  - Reduction in serum Iron, transferrin saturation (TSAT), ferritin
  - Phlebotomy reduction
  - Liver iron content (LIC) by MRI
- Quality of Life (QOL) effects: SF-36, PGI-C

Clinical Study Design:

- Phlebotomy
- Dose: 10 mg, 20 mg, 40 mg, 80 mg
- Weeks: Wk 0, Wk 24
- N = ~28
- Dose ↑ based on TSAT response
PTG-200 AND PN-943
Oral Targeted Investigational Therapies for IBD
IBD: A Growing Multi-Billion Dollar Market
Potential Treatment Paradigm Shift Towards Oral Targeted and Combo Therapy

Current IBD Treatment Paradigm
* **TNF mAbs dominate IBD Therapy**
  - Injectable TNF mAbs – Blockbusters
    - Humira® & Remicade®
    - Global Humira® sales ~ $20 B
  - Significant room for improvement
    - Low response rates
    - Safety concerns - black box warning
    - Lack of convenience

Future of IBD
Oral Combo Therapy?

Injectable mAbs with safer MOAs
1. α4β7 integrin: Entyvio®, Ph2 UC Q4 2020
2. IL-12/IL-23: Stelara®, Ph1 Crohn’s initiated

Oral Targeted Therapy for IBD
Protagonist: *mAb Validated Pathways*
1. **PN-943** (α4β7 integrin)
   - Ph2 UC Q4 2020
2. **PTG-200** (IL-23R, Janssen)
   - Ph2 Crohn’s initiated

Other Oral Approaches: *New Targets*
Small molecule approaches; low barrier to entry
3. **S1P1**: ozanimod, etrasimod
4. **JAK***: Xeljanz®, upadacitinib
   *black box warning*
PTG-200 Partnership with Janssen
IL-23 Receptor Specific Oral Targeted Investigational Therapy for IBD

PTG-200: Potential first-in-class
- Oral, GI-restricted, IL-23 receptor antagonist
- A unique opportunity to extend the Stelara® franchise
- Ph2 Crohn’s study initiated
- Composition of matter patents issued
- Recent conference presentations

Janssen – Protagonist Partnership
- **May 2017**: Partnership initiated; $50M upfront
- **May 2019**: Amended and expanded the collaboration; $25M milestone
- **Jan 2020**: 2nd generation candidate nominated; $5M milestone
- >$1B deal value, up to double digit royalties, US co-detailing rights
  - Research collaboration for 2nd generation compounds
  - Multiple shots on goal approach with increased likelihood of overall success on a risk adjusted basis

Stelara® is a key Janssen franchise
- Approved for Crohn’s & UC
- >$5B total global sales in 2018
PTG-200/JNJ-67864238
Phase 2a PRISM Study in Crohn’s Patients

First Patient Dosed

Moderate to Severe active Crohn’s N=90

Enrollment Criteria:
• Biologics-naïve or failure
• Active Crohn’s Disease - CDAI 220-450

Placebo N= 36 BID

12-week induction study N=90 (3:2 randomization)

Active Drug N= 54 BID

Final Analysis N=90

Primary endpoints:
• ΔCDAI
• Safety & tolerability

Secondary Endpoints:
• SES-CD
• Clinical response
• Endoscopic response
• Endoscopic remission
• Change in patient-reported outcomes
• CRP
• Calprotectin
• PD assays
Oral, $\alpha 4\beta 7$-Specific, GI-Restricted, Targeted Investigational IBD Therapy

**PN-943**

$\alpha 4\beta 7$ integrin: IBD specific, clinically validated target

- IBD specific target
  - T cell homing regulated by interaction between $\alpha 4\beta 7$ integrin and MAdCAM-1
  - MAdCAM-1 expressed only in GI vasculature
- Entyvio (Vedolizumab) approved for Crohn’s & UC
  - ~$3B fiscal 2019 sales
- Superior efficacy for Entyvio vs. Humira in 52 week in Ph3B VARSITY study in UC

**PN-943: Oral intervention of $\alpha 4\beta 7$-MAdCAM-1 pathway**

- First-in-class potential as an oral, GI-restricted $\alpha 4\beta 7$-specific peptide antagonist
  - Ph1 study completed; recent conference presentation
  - Ph2 UC study ready for initiation; COVID-19 related delay
  - Superior potency vs. first candidate PTG-100
    - Observed in preclinical studies
    - PTG-100 showed signals of clinical efficacy in Ph2a UC trial
      - Presented at UEGW, Oct 2018
    - Composition of matter patents issued

PN-943 vs. PTG-100: Ph 1 NHV Single Ascending Dose Study
~3x better Potency based on Dose Related and Saturable Increase in Blood %RO

- PTG-100 showed signals of clinical efficacy in Ph2 PROPEL study in UC patients
  - 44% histological remission based on pre-specified blinded analysis of biopsy samples
  - 16% clinical remission based on blinded endoscopic re-reads with 900 mg q.d. dosing

- PN-943 showed saturable target engagement in Ph1 NHV study
  - Higher %RO confirms superiority to PTG-100 in humans as first observed in preclinical studies

- Next Steps
  - Readiness for Ph2 UC study initiation of PN-943; COVID-19 related delay
PROTAGONIST THERAPEUTICS
Platform, Products, People
Peptide Technology Platform: The Future
Potency, Selectivity, Oral Stability, GI & Systemic Oral Bioavailability

Computational
*Vectrix, Clusters*

Phage Libraries
*Hits*

Peptide Chemistry
*SAR, Leads*

Formulation
*Targeted GI delivery, Oral Bioavailability*

Acidic Stability
Proteases
Peptidases
Lipases

Microbiome
Redox Stability

Oral Stability
*Peptidomimetics, GI Assays*

Potency
Stability

Stability

Targeted GI delivery
Oral Bioavailability
# Protagonist Team

**Experience & Expertise in Innovative Drug Discovery & Development**

<table>
<thead>
<tr>
<th>Company/Role</th>
<th>Name</th>
<th>Title</th>
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<tbody>
<tr>
<td>Bristol-Myers Squibb</td>
<td>Dinesh Patel, PhD</td>
<td>President &amp; CEO</td>
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<tr>
<td>COR</td>
<td>David Liu, PhD</td>
<td>CSO, Head of R&amp;D</td>
</tr>
<tr>
<td>Jazz Pharmaceuticals</td>
<td>Samuel Saks, MD</td>
<td>Chief Medical Officer</td>
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<tr>
<td>alza</td>
<td>Suneel Gupta, PhD</td>
<td>Chief Development Officer</td>
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<tr>
<td>Genentech</td>
<td>Donald Kalkofen</td>
<td>Chief Financial Officer</td>
</tr>
<tr>
<td>UCSF</td>
<td>Tracy Woody</td>
<td>EVP, Corporate Strategy</td>
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<tr>
<td>alza</td>
<td>Ashok Bhandari, PhD</td>
<td>SVP, Discovery Chem &amp; Process Res</td>
</tr>
<tr>
<td>alza</td>
<td>Larry Mattheakis, PhD</td>
<td>SVP, Discovery Biology &amp; Trans Res</td>
</tr>
<tr>
<td>alza</td>
<td>Mohammad Masjedizadeh, PhD</td>
<td>SVP, Pharmaceutical Development</td>
</tr>
<tr>
<td>alza</td>
<td>Abha Bommireddi, MS</td>
<td>SVP, Program Management</td>
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**Protagonist Team**

- Experience & Expertise in Innovative Drug Discovery & Development
## Financials

### Q1 2020

<table>
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<tr>
<th>Description</th>
<th>Amount</th>
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<tr>
<td>Cash &amp; securities at 3/31/2020</td>
<td><strong>$117.5M</strong></td>
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<tr>
<td>Cash, securities and access to debt facility</td>
<td></td>
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<tr>
<td>$50M debt facility with $10M funded</td>
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<tr>
<td>27.4M shares outstanding as of March 31, 2020</td>
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### May 2020

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<th>Description</th>
<th>Amount</th>
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<tr>
<td>Net Offering Proceeds May 2020</td>
<td><strong>$105.9M</strong></td>
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<tr>
<td>Issued 7,000,000 shares at $14.00 per share</td>
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<tr>
<td>Issued additional 1,050,000 underwriter purchase 15% option</td>
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<tr>
<td>Total shares issued 8,050,000</td>
<td></td>
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<tr>
<td>ATM activity</td>
<td><strong>$16.9M</strong></td>
</tr>
<tr>
<td>1.2M Shares issued in May 2020, prior to Offering at average price of $14.02 per share</td>
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<tr>
<td>Total New Capital in May 2020</td>
<td><strong>$122.8M</strong></td>
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<tr>
<td>New shares issued 9.3M</td>
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<tr>
<td>Proforma shares outstanding March 31, 2020 (offering and ATM)</td>
<td>36.7M</td>
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*Refer to the offering circular filed with the SEC on May 11, 2020 for complete offering details.*

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THANK YOU