Corporate and R&D Update
May 7, 2020

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President & CEO, Protagonist Therapeutics
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.

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**Corporate Update**

**Q1 2020**

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

2. **4 Clinical PoC studies in four different diseases**
   - **PTG-300**: *PV selected as the 1st main indication*
   - **PTG-200**: Crohn’s study ongoing
   - **PN-943**: UC study initiation planned

3. **Well financed through mid-2022**
   - End of Q1 2020 cash & investments ~ $117M
PTG-300: A Non-Cytoreductive Hepcidin Hormone Mimetic

Polycythemia Vera as First Indication

First-in-class, non-cytoreductive, synthetic mimetic of the natural hormone hepcidin
Hepcidin is the master regulator of iron homeostasis, storage and distribution in the body

1. Preliminary data: robust clinical responses
   - All dose compliant patients (6 out of 6) are phlebotomy free during 4-28 weeks of treatment to date

2. Orphan regulatory drug development path forward
   - ~100,000 people living in the United States with PV

3. Commercial opportunity
   - Significant unmet need; lack of new non-cytoreductive agents in development
Polycythemia Vera and PTG-300 Study Results
May 7, 2020

Samuel Saks, M.D.,
Chief Medical Officer
Protagonist Therapeutics
Polycythemia Vera and PTG-300 Study Results
May 7, 2020

Ronald Hoffman, M.D.,
Director of the Myeloproliferative Diseases Program
The Icahn School of Medicine at Mount Sinai
What is Polycythemia Vera?

- Myeloproliferative neoplasms are characterized by an abnormal increase in matured blood cells
  - There are approximately 100,000 cases of PV in the US

- Elevated hematocrit is a hallmark of the disease

- Occurs in individuals 50-70 years of age
  - Higher incidence in younger females with life-threatening thrombotic events

- PV patients experience burdensome symptoms

- MPN’s are characterized by three mutations: JAK2, CALR, and MPL
  - The diagnosis of PV almost uniformly (>95%) requires a JAK2 mutation, most often JAK2V617F
Diagnosis, Symptoms and Treatment of PV

• Elevated hematocrit or thrombotic event initiates the diagnosis
  – Followed by blood test to check the presence of a JAK2 mutation
  – Burdensome symptoms include fatigue, headache, visual disturbances, night sweats, and itchiness
  – Thrombotic events is the greatest risk to PV patients
  – Treatment goal is to control hematocrit level below 45%

• Normalization of HCT levels using therapeutic phlebotomy is the most common and first treatment in newly diagnosed PV patients
  – Therapeutic phlebotomy exacerbates iron deficiency contributing to several non-hematological symptoms
  – Cytoreductive therapies such as hydroxyurea and interferon are used in combination with phlebotomy to control HCT
  – Jakafi (ruxolitinib) is the only U.S. FDA approved product for PV

• Significant evidence showing that controlling hematocrit level below 45% is critical to minimizing thrombosis, CV events, and death
Phlebotomy

Efficacy and Side Effects

• Most patients receive low-dose aspirin and undergo phlebotomy with the goals of maintaining hematocrit of <45%

• Patients who undergo phlebotomies will often report feeling tired or dizzy after the phlebotomy, especially in the elderly

• Regular phlebotomy results in iron deficiency that may have debilitating symptoms particularly severe fatigue, weakness, and cognitive impairment

• Three or more phlebotomies in one year while receiving hydroxyurea is associated with worse prognosis

• Hematocrit levels fluctuate between phlebotomy therapy
PTG-300: A Non-Cytoreductive Hepcidin Hormone Mimetic

Mechanism of Action

• Hepcidin hormone has an established role in promoting the sequestration of iron in macrophages decreasing iron availability for production of red blood cells

• PTG-300 is believed to limit excess production of red blood cells in polycythemia vera by removing iron available for red blood cell production

• As a result PTG-300 should not cause the symptoms of true systemic iron deficiency such as those seen in polycythemia vera treated with phlebotomy
PTG-300 Phase 2 Study Design

Part 1 – Dose Finding – 28 Days

Clinically Effective Dose Finding Phase*

- 10 mg
- 20 mg
- 40 mg
- 80 mg

4 to 16 weeks

Efficacy Evaluation Phase**

Dose ± Titration

12 to 24 weeks

Randomized Withdrawal Phase

Fixed Active/Placebo Dose

Up to 12 weeks

Open Label Extension Phase **

Dose ± Titration

Up to 52 weeks

* Titrate every 4 weeks to maintain hematocrit ≤ 45%

**
Therapeutic Phlebotomies Prior to and Post PTG-300 Treatment

Age/Gender | Subject ID | Weeks
---|---|---
74 F | 20 | 40
68 F | 20 | 40
43 M | 20 | 40
71 M | 10 | 20 40 20 20
58 F | 10 | 20 40 80 40 40
52 F | 10 | 20 40
64 F | 10 | 20

Missed one dose due to pandemic

Phlebotomy | First Dose of PTG-300 | Phlebotomy Free | Dose decision(mg)
---|---|---|---
△ | | |
PTG-300 Controls Hematocrit Below 45%
PTG-300 Restores Ferritin to Normal Range

![Graph showing ferritin levels over study weeks](image-url)

- **Study Weeks**: 0, 1, 4, 8, 13, 21
- **FERRITIN (ng/mL)**: 0 to 125
- **Normal Range** indicated on the graph

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[Protagonist Therapeutics logo]

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## PTG-300-04 Study

### Related and Possibly Related Adverse Events

<table>
<thead>
<tr>
<th>Preferred Term</th>
<th>Number of Subjects</th>
<th>Severity Grade</th>
<th>Number of Events</th>
<th>Dose</th>
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<tbody>
<tr>
<td>Injection site reaction</td>
<td>1</td>
<td>1</td>
<td>3</td>
<td>10 mg, 20 mg, 40 mg</td>
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<tr>
<td></td>
<td>1</td>
<td>2</td>
<td>1</td>
<td>20 mg</td>
</tr>
<tr>
<td>Hematoma (bruise)</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>10 mg</td>
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Summary

PTG-300

• Initial data demonstrates the potential of PTG-300 to almost entirely avoid the need for phlebotomy in the treatment of polycythemia vera
  – All dose compliant patients are phlebotomy free to-date (6 out of 6, 4 to 28 weeks of treatment)
  – Persistent control of hematocrit levels to <45%
  – Hematocrit levels above 45% are associated with significant cardiovascular events such as heart attack and stroke

• PTG-300 offers the possibility of weekly administration without the up and down excursions inherent in typical phlebotomy therapy

• The reduction in phlebotomy may allow sufficient iron to be available systemically to avoid symptoms related to iron deficiency

• PTG-300 has potential as the first non-cytoreductive therapy for PV

• PTG-300 was well-tolerated and has a safety profile similar with results of prior studies
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Platelets ($10^3$/uL) Over Time

![Graph showing platelet counts over time for different subjects.](image)

<table>
<thead>
<tr>
<th>Subjects</th>
<th>Dose (mg)</th>
</tr>
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<tbody>
<tr>
<td>1501-01</td>
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</tr>
<tr>
<td>1501-02</td>
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<td>20</td>
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<tr>
<td>1509-01</td>
<td>20</td>
</tr>
</tbody>
</table>
Leukocytes (/uL) Over Time

Subjects | Dose (mg)
--- | ---
1501-01 | 10 10 20 20 20
1501-02 | 10 10 10 10 20
1502-01 | 10 10 20 20 20 40 80 40 40
1502-02 | 10 10 20 20 40 40 20 20
1502-04 | 20
1505-01 | 10 20
1505-02 | 10 20
1509-01 | 10 20