Pioneering new medicines for the treatment of malignant and life-threatening diseases of the bone marrow

February 2021
Investment Highlights

• Novel MOA (LSD1 inhibitor) and potential first-in-class for heme malignancies and solid tumors with opportunity to achieve disease modification

• Clear clinical activity and tolerability with >110 patients treated to date

• Ongoing Phase 2b trials in myelofibrosis (MF) and essential thrombocythemia (ET)

• Multiple clinical readouts in 2021

• Leading investor syndicate including Amgen, Blackrock, Blackstone, Frazier, Farallon, Merck, Omega, Surveyor and T. Rowe Price

• Experienced and accomplished leadership team with multiple exits
Our Pipeline

- **Myelofibrosis (bomedemstat)**: Data updates 2021; Phase 3 FPI 2022
- **Essential Thrombocythemia (bomedemstat)**: Data updates 2021; Phase 3 FPI 2022
- **Polycythemia Vera (bomedemstat)**: Data updates 2021; Phase 3 FPI 2022
- **Myelofibrosis (bomedemstat + ruxolitinib)**: FPI 2021
- **Solid Tumors (NCE, combination)**: Nominate IND candidate
- **Hemoglobinopathies (NCE, combination)**: Enrolling

*FPI: First patient dosed. NCE: New chemical entity.*
Myeloproliferative Neoplasms and Bomedemstat
Myeloproliferative Neoplasms (MPNs)

- Myelofibrosis (MF)
  - Progressive bone marrow failure

- Polycythemia Vera (PV)
  - Excess red cells

- Essential Thrombocythemia (ET)
  - High platelets

Caused by a new mutation in \textit{JAK2} (a kinase), \textit{MPL} (a receptor) or \textit{CALR} (an MPL chaperone).

Results in constitutive activation of the JAK-STAT hematopoietic growth signals.
Strong Rationale for LSD1 Inhibition in MPNs

- LSD1 is an enzyme that removes certain regulatory methyl groups on histones, permitting cell differentiation.
- LSD1 inhibition impairs *malignant* hematopoietic stem cells as well as the function of activated megakaryocytes.
- Megakaryocytes produce the cytokines and growth factors that drive the symptomology of all MPNs, including myelofibrosis.

**Diagram:**
- Inhibition of LSD1
- Extinction of self-renewal
- "Activated" Megakaryocytes
- Myofibroblast
- Extramedullary Hematopoiesis
- Constitutional Symptoms
  - Fatigue
  - Anemia
  - Pain, itching, fever
  - Night sweats
- Bone Marrow Fibrosis
- Splenomegaly
- Reticulin, Collagen
- Growth Factors (e.g., TGFβ1, VEGF, PDGF)
- Inflammatory Cytokines (e.g., IL-8)

**Key Points:**
- LSD1 inhibition reduces production of megakaryocytes, growth factors and cytokines = symptom improvement.
- Potential to extinguish self-renewal of malignant stem cells = potential to improve overall survival.
Bomedemstat: Imago’s novel LSD1 inhibitor

A promising product candidate for the treatment of MPNs

- Discovered by Imago; patent life beyond 2034
- Addresses limitations of other LSD1 inhibitors: superior potency, ADME and designed not to cross blood-brain barrier
- Disease modifying in pre-clinical models
- Demonstrated activity and well-tolerated in >110 patients treated to date; once-daily capsule
- Platelet count is a biomarker of activity on megakaryocytes; provides for individualized titration
- FDA Orphan & Fast Track designation for MF and ET
- EMA Orphan & PRIME designation for MF
Impact of LSD1 Inhibition in Pre-Clinical Models of MPNs

Efficacy of LSD1 inhibition in *Mpl*<sup>W515L</sup> mouse model of MF

In 3 models of MPNs, LSD1 inhibition reduces key hallmarks of disease:

- Spleen and liver volumes
- Leukocytosis and thrombocytosis
- Inflammatory cytokines (e.g., IL-8)
- Growth factors (e.g., VEGF)
- Bone marrow fibrosis
- Mutant cell burden

Maria Kleppe, Ross Levine Lab – Memorial Sloan Kettering
LSD1 Inhibition Lowers Mutant Allele Frequency and Increases Survival

Stem cells in MF murine model at Day 28

Survival of Jak2^{V617F} mice treated with bomedemstat (IMG-7289)

Bone Marrow

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<th>Vehicle</th>
<th>2.5 mpk</th>
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Peripheral Blood

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Overall survival (%)

- Vehicle
- IMG-7289

Day of study

Maria Kleppe, Ross Levine Lab – Memorial Sloan Kettering
Jonas Jutzi, Heike Pahl Lab – University of Freiburg
Working with the World Leaders in MPNs

→ Clinical Investigators, Basic Scientists and Physician Scientists

Scott Armstrong, Dana Farber Cancer Center
• Epigenetics of myeloid disease; collaborator

Claire Harrison, Guy’s and St Thomas’, London
• MF and ET Investigator

Ross Levine, Memorial Sloan Kettering
• MPN genetics; collaborator

Ruben Mesa, University of Texas, San Antonio
• MF and ET investigator

Tim Somervaille, University of Manchester
• LSD1 and myeloid disease; collaborator

Jerry Spivak, Johns Hopkins Hospital
• MPN biology

Moshe Talpaz, University of Michigan
• MF and ET investigator
Myelofibrosis (MF)

MF Overview

- Characterized by progressive bone marrow failure and inflammation due to activating mutations in JAK-STAT pathway
- US prevalence: ~20,000
- Median survival ~5 years
- Significant risk of transformation to AML
- Large QOL impact on patients from splenomegaly and debilitating constitutive symptoms (fatigue, pain, fever, night sweats)

Ruxolitinib

- Pan-JAK inhibitor with clinically meaningful reduction in spleen volume and QOL benefit, yet is not disease modifying
- FDA approval 2011; EMA approval 2012
- Dose limiting side effects and toxicities include anemia, thrombocytopenia, leukopenia and B-cell tumors
- We estimate ~1/3 of MF patients in US are on JAK inhibitor therapy
- Unmet need for all MF patients for a disease modifying therapy and improved symptom relief

Initial addressable market in MF is ~2/3 of patients with platelets ≥ 100K / µL
Bomedemstat in MF: Phase 2a trial in advanced disease

Key Eligibility Criteria
- Are resistant to approved therapies
- Platelets ≥100 \times 10^9/L

Endpoints
- Safety and tolerability
- Symptom reduction (MPN10 SAF TSS)
- Spleen volume reduction (MRI or CT)

Demographics
- 65% had failed multiple agents
- 37% transfusion dependent
- 71% had 2+ mutations of which …
- 73% were high-risk mutations for AML

International trial (N=75)
Bomedemstat in MF: TSS Change at 24 weeks

- 13/16 (81%) had a decrease in TSS
- 6/16 (38%) had a decrease in TSS of ≥50%

Source: Imago preliminary and unaudited Phase 2 data
15/24 (63%) had a decrease in spleen volume @ 12 wks
14/16 (88%) had a decrease in spleen volume @ 24 wks

Source: Imago preliminary and unaudited Phase 2 data
Bomedemstat in MF: Exploratory endpoints

- Heterogenicity among patients evidenced by cytokine expression
- Inflammatory cytokines (S100A9, IL-8, etc.) reduced significantly
- Correlates with reduction in TSS
- May contribute to other clinical benefits including reduction in mutator phenotype and mutant allele frequency

Source: Imago preliminary and unaudited Phase 2 data
Bomedemstat in MF: Reductions in mutant allele frequency

7/22 (32%) show a decrease in some or all somatic mutations

12/22 (55%) have stable MAFs

3/22 (14%) patient have an increased MAFs

- No new mutations identified in patients followed up to 550+ days
- No progression to AML

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Mutations at high risk for developing AML (red)

- No new mutations identified in patients followed up to 550+ days
- No progression to AML

Source: Imago preliminary and unaudited Phase 2 data
Bomedemstat in MF

- Uniquely positioned among all treatments for MPN

- No dose limiting toxicities up to 6 mg/kg
- No safety signals in >4 years
- No genotoxicity
- No deaths related to study drug
- Out of 917 AEs reported, 307 attributed to bomedemstat
- The most common non-hematologic AE related to bomedemstat was dysgeusia (35%) - essentially all Grade 1
- Overall excellent safety and tolerability profile

- 6 SAEs attributed by Investigators as possibly related to bomedemstat (1 Grade 2, 5 Grade 3)
  - Painful splenomegaly
  - Vertigo
  - Headache
  - Heart failure
  - Rectal bleeding
  - Upper GI bleeding

Source: Imago preliminary and unaudited Phase 2 data
Essential Thrombocytethemia (ET)

ET Overview

- Characterized by elevated platelets (often $10^6/\mu\text{L}$ or greater)
- US prevalence: ~125,000
- Significant morbidity and mortality due to thrombotic events and progression to AML
- Risk stratification based on age, history of thrombotic events, JAK mutation status
  - Very low risk – 35,750 patients
  - Low risk – 28,600 patients
  - Intermediate risk – 21,450 patients
  - High risk – 57,200 patients

Current treatments

- Cytoreductive therapy, most often with hydroxyurea (HU), is indicated for all high-risk patients
- Significant unmet need for 20-25% of treated patients who become intolerant or resistant to HU
- Anagrelide, pegylated interferon alpha and busulfan may be used despite their toxicities

Bomedemstat initial addressable market: ET patients intolerant of or resistant to HU
Bomedemstat in ET: Phase 2 trial design

- FDA cleared in 2019; FPFV July 2020
- Up to 60 high-risk ET patients
- Single arm, open-label boomedemstat once-daily
- ~25 sites in US, UK, EU, AUS and NZ

Primary objectives
- Safety and tolerability
- Reduction of platelet count to ≤400K/μL in the absence of thromboembolic events

Secondary objectives
- Reduction in mutant allele frequency (MAF)
- Reduced event rate (thrombosis and hemorrhage)
- Reduced progression to MF and AML
Bomedemstat in ET: lowers platelets

Proof of principle achieved in Phase 2 Trial

- All patients showed reduction in platelets
- Dosages in same range as for MF
- Individual dosing allows maximum benefit while minimizing AEs

Source: Imago preliminary and unaudited Phase 2 data
Bomedemstat in ET: maintains Hb and controls WBCs

**Phase 2: White Blood Cells**

- 055-210
- 001-201
- 055-202
- 012-201
- 001-202
- 003-201
- 055-203
- 056-201
- 009-201
- 006-201
- 057-201

**Phase 2: Hemoglobin**

- 055-210
- 001-201
- 055-202
- 012-201
- 001-202
- 003-201
- 055-203
- 056-201
- 009-201
- 006-201
- 057-201

Source: Imago preliminary and unaudited Phase 2 data
Leadership

Management

Hugh Y. Rienhoff, Jr., MD
Founder, CEO

Laura G. Eichorn
COO

Jennifer Peppe
SVP, Clinical Operations

Matthew Plunkett, PhD
CFO

Amy E. Tapper, PhD
SVP, Non-clinical and CMC

Board

Dennis Henner, PhD (Chair)

Robert Baltera

Dina Chaya, PhD

Enoch Kariuki, PharmD

Patrick Heron

Hugh Y. Rienhoff, Jr., MD

Harish Soundararajan, PhD
Experienced public, private and strategic investors

$80 million Series C, led by Farallon, completed November 2020
Pipeline and upcoming milestones

<table>
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<tr>
<th>Disease</th>
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<th>Phase 2</th>
<th>Phase 3</th>
<th>Next Anticipated Milestone(s)</th>
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Data presentations anticipated at major medical meetings in 2021
Regulatory updates, including End-of-Phase 2 meetings, prior to pivots

FPI: First patient dosed. NCE: New chemical entity.
Thank you