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ELEVENTH ANNUAL MEETING

TARGETED THERAPY OF UNCONTROLLED ERYTHROCYTOSIS IN POLYCYTHEMIA VERA WITH THE HEPCIDIN MIMETIC, RUSFERTIDE: BLINDED RANDOMIZATED WITHDRAWAL RESULTS OF THE PHASE 2 REVIVE STUDY.

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Protagonist Therapeutics

INTRODUCTION

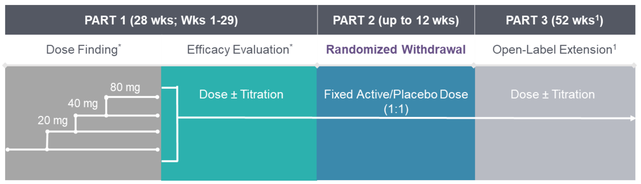
- Polycythemia Vera (PV) is a myeloproliferative neoplasm characterized by excessive production of red blood cells (RBCs).[1] Elevated hematocrit (HCT) is a hallmark of PV.[2] Uncontrolled HCT is associated with higher rates of death from cardiovascular causes (CV) or thrombotic events(TE).[3] Maintaining HCT<45% is critical in PV to decrease the risk of TE and CV events (NCCN and ELN guidelines). Current standard of care does not maintain HCT <45% at all times in a majority of patients.[4,5]
- Hepcidin is a peptide hormone, produced by the liver and is the body's main regulator of iron homeostasis. Hepcidin controls the availability of iron for formation of RBCs. Rusfertide is a novel investigational peptidic hepcidin mimetic.

AIM

- The REVIVE Phase 2 study (NCT04057040) evaluated the safety and efficacy of rusfertide in patients with polycythemia vera who had a high phlebotomy burden while on standard of care therapy.

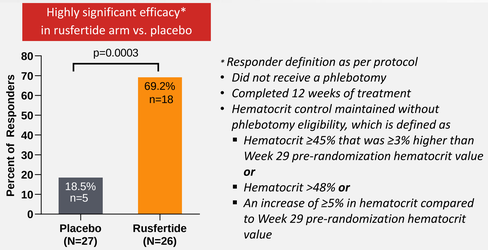
METHOD

- The REVIVE trial consists of three stages.
  - During Part 1 (28 weeks), rusfertide dose was adjusted individually to control HCT <45%.
  - During Part 2 (week 29-41), the blinded randomized withdrawal phase, patients were randomized to either continue rusfertide or to matching placebo.
  - Part 3 is a 3-yr open-label extension.
- Eligibility criteria: ≥3 therapeutic phlebotomies (TP) in the 28 weeks prior to enrollment with or without concurrent cytoreductive therapy.



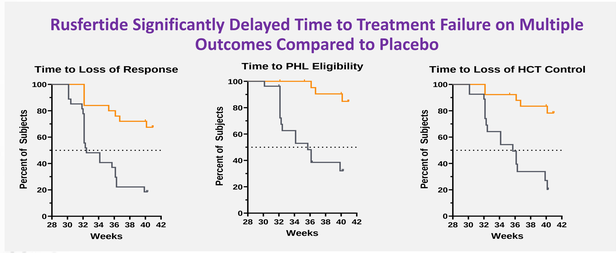
*Titrate every 4 weeks to maintain HCT <45%.

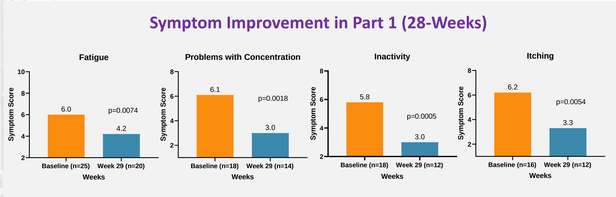
RESULTS



*Responder definition as per protocol
- Did not receive a phlebotomy
- Completed 12 weeks of treatment
- Hematocrit control maintained without phlebotomy eligibility, which is defined as
  - Hematocrit ≥45% that was ≥3% higher than Week 29 pre-randomization hematocrit value **or**
  - Hematocrit >48% **or**
  - An increase of ≥5% in hematocrit compared to Week 29 pre-randomization hematocrit value

- **69.2% of subjects** (18 out of 26) are responders. 8 non-responders as per protocol definition.
- 3 fulfilled the phlebotomy eligibility criteria
- 5 discontinued treatment per patient/investigator discretion
- All 8 non-responders continued in the Part 3 open-label extension part of the study
- 7 out of the 8 subjects continued treatment into Part 3
- **92.3% of subjects** (24 out of 26) in rusfertide arm did not receive phlebotomy in Part 2, the 12-week randomization part of the study





TEAEs by Preferred Term Noted at ≥15%	N=70
Subjects with at least one TEAE	70 (100%)
Injection site erythema	46 (66%)
Injection site pain	29 (41%)
Injection site pruritus	28 (40%)
Fatigue	23 (33%)
Injection site mass	19 (27%)
Pruritus	19 (27%)
Arthralgia	18 (26%)
Injection site swelling	18 (26%)
Headache	18 (26%)
Nausea	18 (26%)
COVID-19	17 (24%)
Dizziness	17 (24%)
Anemia	14 (20%)
Injection site irritation	13 (19%)
Injection site bruising	12 (17%)
Dyspnea	11 (16%)

Safety data as of 11 July 2023

CONCLUSIONS

- The REVIVE study demonstrated a significantly higher efficacy with rusfertide compared to placebo in subjects with PV during the blinded randomization withdrawal.
- The study met the efficacy endpoints (Proportion of Responders, Absence of phlebotomy eligibility, Hematocrit control).
- Rusfertide demonstrated favorable effects on several Patient-Reported Outcomes (fatigue, problems with concentration, pruritus, inactivity), in patients who were burdened by these symptoms.
- Rusfertide was generally well tolerated. TEAEs were generally Grade 1 or 2. The most common TEAEs was ISRs. There were no Grade 4 or 5 TEAEs.
- Current standard of care therapy in PV does not consistently maintain hematocrit <45%, thereby potentially increasing the risk of thromboembolic events. Rusfertide has the potential to consistently maintain hematocrit <45%.
- Rusfertide is currently being investigated in the ongoing placebo-controlled VERIFY Phase 3 study (NCT05210790).
- A separate follow-on 2-year extension study will start later this year for patients who complete participation in the REVIVE study.

REFERENCES

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CONTACT INFORMATION

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