



Geron Announces IMerge Phase 3 Presentations at ASH Highlighting Significant Durability of Transfusion Independence and Breadth of Effect Across MDS Subgroups with Imetelstat in Lower Risk MDS

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- *Imetelstat is currently under regulatory review by the FDA and EMA for the treatment of transfusion-dependent anemia in adult patients with lower risk MDS*

FOSTER CITY, Calif.--(BUSINESS WIRE)-- Geron Corporation (Nasdaq: GERN), a late-stage clinical biopharmaceutical company, today announced presentations of data from its IMerge Phase 3 clinical trial evaluating first-in-class investigational telomerase inhibitor imetelstat in patients with lower risk myelodysplastic syndromes (MDS), as well as population analysis of claims data in lower risk MDS. The data were presented at the American Society of Hematology (ASH) Annual Meeting, taking place from December 9-12, 2023, in San Diego, CA and virtually as well as published online in *Blood*.

"These latest analyses from IMerge Phase 3 presented at ASH contribute to a growing body of data from the trial, including a recent publication in *The Lancet*, which continue to give us confidence in what we believe is a meaningful clinical benefit with imetelstat in these lower risk MDS patients," said Faye Feller, M.D., Executive Vice President, Geron's Chief Medical Officer. "If approved, we believe that the significant improvement in red blood cell transfusion independence possible with imetelstat could provide an important new treatment option for many lower risk MDS patients who suffer from iron overload and low quality of life associated with transfusion dependence."

"As we continue to see additional analyses from IMerge Phase 3, such as these latest presentations at ASH, the clinical attributes of imetelstat continue to be differentiated, particularly high RBC-TI response rate, durability of response and the consistency of effect across MDS subgroups that have historically been very difficult to treat," said Amer Methqal Zeidan, MBBS MHS, Associate Professor of Internal Medicine (Hematology) and director of hematology Early Therapy Research at Yale School of Medicine and Yale Cancer Center, who is an IMerge lead investigator. "Additionally, the safety profile was well-characterized, with Grade 3/4 neutropenia and thrombocytopenia that were generally transient, reversible to Grade 2 or less, and clinically manageable, and most importantly, had few clinical consequences and did not affect the efficacy of imetelstat."

Below are the highlights of the 6 company-sponsored abstracts:

"Efficacy of Imetelstat in Achieving Red Blood Cell Transfusion Independence Across Different Risk Subgroups in Patients With Lower-Risk Myelodysplastic Syndromes Relapsed/Refractory to Erythropoiesis-Stimulating Agents in IMerge Phase 3 Study"

This oral presentation provides a subgroup analysis from IMerge Phase 3 evaluating RBC-transfusion independence (RBC-TI) rates in patients treated with imetelstat vs. placebo across different risk subgroups as defined by International Prognostic Scoring System (IPSS), revised IPSS (IPSS-R) or IPSS molecular (IPSS-M) risk profiles. The results showed that imetelstat consistently had higher RBC-TI response rates than placebo across these different risk subgroups. Overall, durable 24-week and 1-year RBC-TI responses were observed with imetelstat in all lower- and higher-risk subgroups. Reclassifying patients by IPSS-M revealed that one-third of the patients (4/12) identified as higher-risk IPSS-M derived 8-week RBC-TI benefit whereas higher-risk subgroups receiving placebo failed to achieve long-term RBC-TI, regardless of the risk classification scheme used.

"Impact of Mutational Status on Clinical Response to Imetelstat in Patients with Lower Risk Myelodysplastic Syndromes in the IMerge Phase 3 Study"

This poster evaluates the impact of MDS-associated mutations on clinical efficacy of imetelstat for the 165 of 178 patients for whom mutation data were available. Results showed that in patients who had more than one mutation detected at baseline and more than two mutations at baseline, imetelstat significantly improved the 8-week and 24-week RBC-TI response rates compared with placebo. A significantly higher percentage of imetelstat-treated than placebo-treated patients with baseline mutations in *SF3B1*, a gene commonly mutated in MDS, achieved 8- and 24-week RBC-TI. RBC-TI responses in patients receiving imetelstat occurred regardless of the presence of mutations associated with poor prognosis or the number of mutations. This analysis suggests clinical benefit of imetelstat across different molecularly defined subgroups and independent of the underlying molecular mutation pattern.

"Durable Continuous Transfusion Independence With Imetelstat in IMerge Phase 3 for Patients With Heavily Transfused Non-Del(5q) Lower-Risk Myelodysplastic Syndromes Relapsed/Refractory to or Ineligible for Erythropoiesis-Stimulating Agents"

This poster reports on the patients enrolled in IMerge Phase 3 who achieved one-year or greater continuous RBC-TI response, which included 17.8% of imetelstat-treated patients (21/118; 95% CI, 11.4-25.9) and 1.7% of patients on placebo (1/60; 95% CI,

0-8.9). One-year RBC-TIs were achieved by 44.7% of 8-week RBC-TI responders and 63.6% of 24-week RBC-TI responders. During the one-year or greater RBC-transfusion-free interval, RBC transfusion burden was reduced from a baseline range of 4-9 units and hemoglobin improved a median of 5.2 g/dL. Imetelstat 1-year RBC-TI responders had a median duration of RBC-TI of 123 weeks (95% CI, 80.4-NE) and no patients progressed to acute myeloid leukemia (AML). At the time of data cutoff (May 10, 2023), 13 1-year RBC-TI responders receiving imetelstat and one patient receiving placebo were ongoing on treatment. Of the 18 imetelstat one-year responders for whom mutational data were available, complete elimination of certain mutational clones was observed in 10 of 18 patients (55.5%) for whom mutational data were available and 13 (72.2%) achieved greater than or equal to 50% *SF3B1* variant allele frequency (VAF) reduction, including 7 patients with complete elimination of VAF. For these one-year RBC-TI responders and consistent with the overall safety profile for patients on IMerge Phase 3, Grade 3-4 thrombocytopenia and neutropenia occurred in 14 (67%) and 20 (95%) patients, with a mean duration of 1.78 (1.58) and 2.25 (2.48) weeks, respectively. 81% of Grade 3-4 neutropenia and 89% of Grade 3-4 thrombocytopenia were reversible to Grade 2 or below within 4 weeks.

"Improvement of Patient-Reported Outcomes Among Heavily Pretreated Patients With Lower-Risk Myelodysplastic Syndromes and High Transfusion Burden Treated With Imetelstat on the IMerge Phase 3 Trial"

This abstract published in *Blood* describes exploratory results from patient-reported outcomes (PROs) questionnaires used in IMerge Phase 3. Functional Assessment of Cancer Therapy-Anemia (FACT-An; 55 items) and Quality of Life in Myelodysplasia Scale (QUALMS; 38 items) were the main questionnaires used. Findings consistently showed that imetelstat-treated patients reported improved fatigue, dyspnea, and QUALMS composite scores (total and physical burden) compared to those on placebo. Further, patients treated with imetelstat did not experience greater deterioration in systemic symptoms, pain, physical function or bleeding than those on placebo. These data indicate that, in addition to improving RBC transfusion burden in patients with LR MDS, imetelstat targets multiple core symptoms of LR MDS simultaneously, also improving those respective PROs.

"Characterization and Management of Cytopenias after Imetelstat Treatment in the IMerge Phase 3 Trial of Patients with Lower-Risk Myelodysplastic Syndromes (LR-MDS)"

This abstract published in *Blood* describes treatment-emergent adverse events (TEAEs) of grade 3 or 4 thrombocytopenia and neutropenia, which were more prevalent in cycles 1-3 (68.6% and 62.7% respectively), and their frequency decreased over time. In the imetelstat group, cytopenias were managed with protocol-specified treatment delays and dose adjustments. Dose reductions due to neutropenia and thrombocytopenia occurred in 33.1% and 22.9% of patients, respectively. Thrombocytopenia and neutropenia were also managed by cycle delays in 46.6% and 50.8% of patients, by platelet transfusions in 17.8% of patients, and by concomitant therapy with growth factor support (mostly during cycles 2-4) in 34.7% of patients. Among 47 patients who achieved the primary endpoint of 8-week RBC-TI with imetelstat, 72.3% and 59.6% of patients had grade 3 or 4 neutropenia and thrombocytopenia, respectively. This analysis shows that these Grade 3 or 4 thrombocytopenia and neutropenia were generally transient, reversible and manageable through treatment delays and dose adjustments, and suggests that these TEAEs do not affect the efficacy of imetelstat.

A Geron-sponsored population analysis of claims data also were presented in poster format.

"Durable Transfusion Independence in Lower Risk Myelodysplastic Syndrome (LR MDS) Is Associated with Better Survival: A Population Level Analysis Based on a Large US Health Insurance Claims Database"

This poster describes a population level analysis of 5,662 lower risk MDS patients identified through Optum Clinformatics® between October 2015 and June 2022. In these patients, real-world progression-free survival (rwPFS) from the start of first- and second- line therapy respectively, was significantly longer in patients who achieved 16-week RBC-TI after treatments than in patients who did not ($p < .0001$). RBC-TI responders also had significantly greater improvement in median overall survival (OS) from first and second line than non-responders ($p < .0001$ for both). This analysis indicates that achievement of RBC-TI was associated with improved survival, suggesting that transfusion dependence is a modifiable predictor of clinical outcomes in lower risk MDS.

The presentation and posters are available on the [Publications Section](#) of Geron's corporate website and the abstracts are available online in [Blood](#).

About IMerge Phase 3

The Phase 3 portion of the IMerge Phase 2/3 study is a double-blind, 2:1 randomized, placebo-controlled clinical trial to evaluate imetelstat in patients with IPSS Low or Intermediate-1 risk (lower risk) transfusion dependent MDS who were relapsed after, refractory to, or ineligible for, erythropoiesis stimulating agent (ESA) treatment, had not received prior treatment with either a HMA or lenalidomide and were non-del(5q). To be eligible for IMerge Phase 3, patients were required to be transfusion dependent, defined as requiring at least four units of packed red blood cells (RBCs), over an eight-week period during the 16 weeks prior to entry into the trial. The primary efficacy endpoint of IMerge Phase 3 is the rate of red blood cell transfusion independence (RBC-TI) lasting at least eight weeks, defined as the proportion of patients without any RBC transfusion for at least eight consecutive weeks since entry to the trial (8-week RBC-TI). Key secondary endpoints include the rate of RBC-TI lasting at least 24 weeks (24-week RBC-TI), the duration of RBC-TI and the rate of hematologic improvement erythroid (HI-E), which is defined under 2006 IWG criteria as a rise in hemoglobin of at least 1.5 g/dL above the pretreatment level for at least eight weeks or a reduction of at least four units of RBC transfusions over eight weeks compared with the prior RBC transfusion burden. A total of 178 patients were enrolled in IMerge Phase 3 across North America, Europe, Middle East and Asia.

About Imetelstat

Imetelstat is a novel, first-in-class investigational telomerase inhibitor exclusively owned by Geron and being developed in hematologic malignancies. Data from non-clinical studies and clinical trials of imetelstat provide strong evidence that imetelstat targets telomerase to inhibit the uncontrolled proliferation of malignant stem and progenitor cells in myeloid hematologic malignancies resulting in malignant cell apoptosis and potential disease-modifying activity. Imetelstat has been granted Fast Track designation by the U.S. Food and Drug Administration for both the treatment of adult patients with transfusion dependent anemia due to Low or Intermediate-1 risk MDS that is not associated with del(5q) who are refractory or resistant to an erythropoiesis stimulating agent, and for adult patients with Intermediate-2 or High-risk myelofibrosis (MF) whose disease has relapsed after or is refractory to janus associated kinase (JAK) inhibitor treatment. Imetelstat is currently not approved by any regulatory authority.

About Geron

Geron is a late-stage clinical biopharmaceutical company pursuing therapies with the potential to extend and enrich the lives of patients living with hematologic malignancies. Our first-in-class investigational telomerase inhibitor, imetelstat, harnesses Nobel Prize-winning science in a treatment that may alter the underlying drivers of disease. The New Drug Application (NDA) for imetelstat for the treatment of transfusion dependent anemia in adult patients with lower risk myelodysplastic syndromes (LR MDS) who have failed to respond or have lost response to or are ineligible for erythropoiesis-stimulating agents (ESAs), based on the results from the Phase 3 IMerge clinical trial, is currently under review by the United States Food and Drug Administration (FDA) with a Prescription Drug User Fee Act (PDUFA) target action date of June 16, 2024. In addition, an MAA is under review in the European Union for the same proposed indication. Furthermore, Geron currently has an ongoing pivotal Phase 3 clinical trial evaluating imetelstat in relapsed/refractory myelofibrosis (MF). To learn more, visit www.geron.com or follow us on [LinkedIn](#).

Use of Forward-Looking Statements

Except for the historical information contained herein, this press release contains forward-looking statements made pursuant to the "safe harbor" provisions of the Private Securities Litigation Reform Act of 1995. Investors are cautioned that such statements, include, without limitation: (i) that data from the IMerge Phase 3 clinical trial presented at ASH continue to suggest a meaningful clinical benefit with imetelstat in patients with lower risk MDS, and that if approved, imetelstat could provide an important new treatment option for many lower risk MDS patients; (ii) that, with additional analyses from IMerge Phase 3, such as the latest presentations at ASH, the clinical attributes of imetelstat continue to be differentiated; (iii) that data from IMerge Phase 3 presented at ASH suggests clinical benefit of imetelstat across different molecularly defined subgroups and independent of the underlying molecular mutation pattern; (iv) that data from a large U.S. health insurer claims database presented at ASH indicates that achievement of RBC-TI was associated with improved survival, suggesting that transfusion dependence is a modifiable predictor of clinical outcomes in lower risk MDS; (v) that data from a patient-reported outcomes (PROs) study presented at ASH indicate that, in addition to improving RBC transfusion burden in patients with LR-MDS, imetelstat targets multiple core symptoms of LR-MDS simultaneously, also improving those PROs; (vi) that data presented at ASH shows that Grade 3 or 4 thrombocytopenia and neutropenia experienced by imetelstat-treated patients were generally transient, reversible and manageable through treatment delays and dose adjustments, and suggests that these TEAEs do not affect the efficacy of imetelstat; and (vii) other statements that are not historical facts, constitute forward-looking statements. These forward-looking statements involve risks and uncertainties that can cause actual results to differ materially from those in such forward-looking statements. These risks and uncertainties, include, without limitation, risks and uncertainties related to: (a) whether regulatory authorities permit the further development of imetelstat on a timely basis, or at all, without any clinical holds; (b) whether any future safety or efficacy results cause the benefit-risk profile of imetelstat to become unacceptable; (c) whether imetelstat actually demonstrates that it alters the underlying drivers of disease and has disease-modifying activity in patients; and (d) whether the FDA and EMA will approve imetelstat for the treatment of transfusion-dependent anemia in patients with lower risk MDS. Additional information on the above risks and uncertainties and additional risks, uncertainties and factors that could cause actual results to differ materially from those in the forward-looking statements are contained in Geron's filings and periodic reports filed with the Securities and Exchange Commission under the heading "Risk Factors" and elsewhere in such filings and reports, including Geron's quarterly report on Form 10-Q for the quarter ended September 30, 2023 and future filings and reports by Geron. Undue reliance should not be placed on forward-looking statements, which speak only as of the date they are made, and the facts and assumptions underlying the forward-looking statements may change. Except as required by law, Geron disclaims any obligation to update these forward-looking statements to reflect future information, events or circumstances.

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