Geron Announces New Data and Analyses from IMerge Phase 3 Presented at EHA Reporting Robust Durability of Transfusion Independence, Evidence of Disease-Modifying Activity and Favorable Fatigue PRO in Imetelstat-Treated Lower Risk MDS Patients

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- New analyses from IMerge Phase 3 reported higher 24-week transfusion independence (TI) responses for imetelstat-treated patients vs. placebo across key myelodysplastic syndromes (MDS) subgroups and across spectrum of MDS mutations
- New data and analyses indicated greater variant allele frequency (VAF) reductions for imetelstat-treated patients vs. placebo across multiple genes commonly mutated in MDS; these reductions also were correlated with clinical endpoints of TI response, longer TI duration and increase in hemoglobin levels, providing further evidence of disease-modifying activity of imetelstat
- First data on patient-reported outcomes (PRO) described a sustained meaningful improvement in fatigue for imetelstat-treated patients vs. placebo
- Data support NDA submission, which is on track for June 2023 to support potential U.S. commercial launch in first half of 2024

FOSTER CITY, Calif.--(BUSINESS WIRE)-- Geron Corporation (Nasdaq: GERN), a late-stage clinical biopharmaceutical company, today announced new data and analyses from IMerge Phase 3 reporting robust durability of transfusion independence (TI), evidence for disease-modifying activity and favorable fatigue patient-reported outcomes (PRO) in lower risk myelodysplastic syndromes (MDS) patients treated with the Company's first-in-class telomerase inhibitor, imetelstat, vs. placebo. The data and analyses were presented at the European Hematology Association (EHA) Annual Meeting, which took place from June 8-11, 2023 in Frankfurt, Germany and virtually.

"The new IMerge Phase 3 data and analyses presented at EHA continue to support the unprecedented and differentiating attributes of imetelstat, including 24-week transfusion independence across key MDS subgroups, potential disease-modifying activity, as well as favorable patient-reported outcomes (PRO) data on meaningful improvement in fatigue," said Faye Feller, M.D., Executive Vice President, Chief Medical Officer of Geron. "Each of these qualities address important unmet needs for lower risk MDS patients due to the limitation of current treatment options. Submission of our New Drug Application later this month is a significant step to hopefully bring imetelstat to these transfusion burdened patients."

Presentation Title: Continuous Transfusion Independence with Imetelstat in Heavily Transfused Non-Del(5q) Lower Risk Myelodysplastic Syndromes Relapsed/Refractory to Erythropoiesis Stimulating Agents in IMerge Phase 3

Top-line results from the primary analysis of IMerge Phase 3 **presented** earlier this month at the 2023 American Society of Hematology (ASCO) Annual Meeting were also covered in the EHA presentation, including the primary endpoint of 8-week transfusion independence (TI) and key secondary endpoint of 24-week TI were met with high statistical significance (P<0.001) for imetelstat-treated patients vs. placebo. Further, mean hemoglobin levels in imetelstat-treated patients increased significantly (P<0.001) over time compared to placebo patients.

In addition to these results, the EHA presentation also provided new data and analyses highlighting clinically meaningful and durable TI for imetelstat-treated patients vs. placebo. As of a January 2023 data cut-off, 17.8% (21/118) of imetelstat-treated patients vs. 1.7% (1/60) of placebo-treated patients achieved 1-year TI (P=0.002), representing 63.6% of 24-week TI imetelstat responders.

Two new analyses presented at EHA on TI responses by subgroups underscored the breadth of potential effect of imetelstat vs. placebo. The first analysis reported higher durability of TI for imetelstat-treated patients vs. placebo across key MDS subgroups:

Durability of RBC-TI for 8-Week TI Responders Across Key LR MDS Subgroups

	Imetelstat median, weeks (95% CI)	Placebo median, weeks (95% CI)	Hazard ratio (95% CI)	P-value
Overall	51.6 (26.9–83.9)	13.3 (8.0–24.9)	0.23 (0.09–0.57)	<0.001
WHO category				
RS+	46.9 (25.9–83.9)	16.9 (8.0–24.9)	0.32 (0.11–0.95)	0.035
RS-	51.6 (11.9–NE)	11.2 (10.1–NE)	0.11 (0.01–1.43)	0.062
Prior RBC transfusion burden per IWG 2006				
4–6 units/8 weeks	51.9 (24.9–122.9)	16.9 (10.1–24.9)	0.35 (0.13–0.96)	0.035
6 units/8 weeks	39.9 (15.9–NE)	8.4 (8.0–NE)	0.04 (0.003–0.48)	<0.001
IPSS risk category				
Low	43.9 (25.0–NE)	15.1 (8.0–24.9)	0.26 (0.10–0.68)	0.004
Intermediate-1	51.6 (11.9–NE)	10.1 (NE–NE)	0.15 (0.01–2.47)	0.128
Baseline sEPO				
≤500 mU/mL	51.6 (26.9–83.9)	13.3 (8.0–24.9)	0.21 (0.075–0.61)	0.002
>500 mU/mL	122.9 (8.14–NE)	14.6 (12.3–NE)	0.34 (0.03–3.85)	0.364
Prior ESA use				
Yes	43.9 (26.9–80.0)	13.3 (8.0–24.9)	0.26 (0.10–0.72)	0.006
No	122.9 (8.14–NE)	14.6 (12.3–NE)	0.34 (0.03–3.85)	0.364

Data cut-off: October 13, 2022.
Hazard ratio (95% CI) from the Cox proportional hazard model, stratified by prior RBC transfusion burden (≥4 to ≤6 vs >6 RBC units/8 weeks during a 16-week period prior to randomization) and baseline IPSS risk category (low vs intermediate-1), with treatment as the only covariate. P-value (2-sided) for superiority of imetelstat vs placebo in hazard ratio based on stratified log-rank test.
ESA, erythropoiesis-stimulating agent; IPSS, International Prognostic Scoring System; IWG, International Working Group; LR-MDS, lower-risk myelodysplastic syndromes; NE, not estimable; RBC, red blood cell; RS, ring sideroblast; sEPO, serum erythropoietin; TI, transfusion independence.

The second analysis reported higher 24-week TI for imetelstat-treated patients vs. placebo across key MDS subgroups:

Comparable 24-Week RBC-TI Rate Across Key LR MDS Subgroups

	Imetelstat n/N (%)	Placebo, n/N (%)	% Difference (95% CI)	P-value
Overall	33/118 (28.0)	2/60 (3.3)	24.6 (12.64–34.18)	<0.001
WHO category				
RS+	24/73 (32.9)	2/37 (5.4)	20.5 (−0.03–35.75)	0.003
RS-	9/44 (20.5)	0/23 (0.0)	0.11 (0.01–1.43)	0.019
Prior RBC transfusion burden per IWG 2006				
4–6 units/8 weeks	19/62 (30.6)	2/33 (6.1)	24.6 (5.68–38.66)	0.006
6 units/8 weeks	39.9 (15.9–NE)	8.4 (8.0–NE)	0.04 (0.003–0.48)	<0.001
IPSS risk category				
Low	23/80 (28.8)	2/39 (5.1)	23.6 (7.23–35.75)	0.003
Intermediate-1	10/38 (26.3)	0/21 (0)	26.3 (3.46–43.39)	0.009
Baseline sEPO				
≤500 mU/mL	29/87 (33.3)	2/36 (5.6)	27.8 (10.46–39.71)	0.002
>500 mU/mL	4/26 (15.4)	0/22 (0)	15.4 (−5.81–35.73)	0.050
Prior ESA use				
Yes	31/108 (28.7)	2/52 (3.8)	24.9 (11.61–35.00)	<0.001
No	2/10 (20)	0/8	20.0 (-23.47–55.78)	0.225

Data cut-off: October 13, 2022.
95% CI based on Wilson Score method. P-value determined by the Cochran-Mantel-Haenszel test, with stratification for prior RBC transfusion burden (≥4 to ≤6 vs >6 RBC units/8 weeks during a 16-week period prior to randomization) and baseline IPSS risk category (low vs intermediate-1) applied to randomization.
ESA, erythropoiesis-stimulating agent; IPSS, International Prognostic Scoring System; IWG, International Working Group; LR-MDS, lower-risk myelodysplastic syndromes; RBC, red blood cell; RS, ring sideroblast; sEPO, serum erythropoietin; TI, transfusion independence.

Additionally, the rate of 24-week TI was higher with imetelstat vs. placebo regardless of baseline mutation status, telomerase activity (TA), telomerase length (TL), and human telomerase reverse transcriptase (hTERT).

“For the first time at EHA, we see comparable 24-week TI across key MDS subgroups, which is especially meaningful for patients without ring sideroblasts (RS-) and very heavily transfusion burdened patients, who particularly have limited options today,” said Uwe Platzbecker, M.D., Department of Hematology, Cellular Therapy and Hemostaseology, Leipzig University Hospital, Leipzig, Germany, who presented the data at EHA and is an IMerge investigator. “In addition to the durability of TI, imetelstat-treated patients also achieved significant increases in hemoglobin and reductions of transfusion units that could be life changing for lower risk MDS patients, who often present with symptomatic anemia and transfusion dependence.”

As previously reported, the safety profile observed with imetelstat in IMerge Phase 3 was consistent with prior clinical experience with no new safety signals. The EHA presentation provided new data on the consequences of the grade 3-4 thrombocytopenia and neutropenia which were most often reported during Cycles 1-3 and led to dose modifications. While approximately 50% of patients treated with imetelstat had dose reductions due to treatment emergent adverse events (TEAE), less than 15% of patients discontinued treatment due to TEAE. Discontinuation of

imetelstat treatment in these patients due to a TEAE generally occurred late in treatment, with a median time to treatment discontinuation of 21.1 weeks (range 2.3 to 44.0 weeks).

Presentation Title: Disease-Modifying Activity of Imetelstat in Patients with Heavily Transfused Non-Del(5q) Lower Risk Myelodysplastic Syndromes Relapsed/Refractory to Erythropoiesis Stimulating Agents in IMerge Phase 3

“In IMerge Phase 3, not only did we observe efficacy with imetelstat across the spectrum of genetic mutations associated with lower risk MDS, but we also saw a reduction in mutation burden, as measured by variant allele frequency (VAF). Furthermore, greater reduction of VAF in multiple genes correlated with the clinical endpoints of TI response, longer TI duration and increase in hemoglobin levels, suggesting the potential of imetelstat to modify the disease. This is the first therapy we know of that may alter the underlying biology of lower risk MDS by potentially reducing or eliminating malignant clones and improving ineffective erythropoiesis,” said Valeria Santini, M.D., MDS Unit, Azienda Ospedaliero Universitaria Careggi, University of Florence, Florence, Italy, who presented the data at EHA and is an IMerge investigator.

In the EHA presentation, new data on cytogenetic responses and reductions in bone marrow RS supported the telomerase inhibition mechanism of action (MOA) of imetelstat. Among patients with cytogenetic abnormalities at baseline, the cytogenetic response rate was 35% (9/26) in imetelstat-treated patients and 15% (2/13) in the placebo group. Among cytogenetic responders, 89% (8/9) of patients in the imetelstat group and 50% (1/2) in the placebo group also achieved 8-week TI. A higher percentage of patients treated with imetelstat (40.8%) vs. placebo (9.7%) had a ≥50% reduction in central bone marrow RS. TI responses were enriched in patients achieving a ≥50% reduction in central bone marrow RS.

Furthermore, the EHA presentation provided updated data on VAF reductions and new analyses on the correlation of such reductions with clinical responses which further support the potential disease-modifying activity of imetelstat. Reductions in variant allele frequency (VAF) of genes frequently mutated in MDS were greater for imetelstat-treated patients than placebo: SF3B1 (P< 0.001), TET2 (P= 0.032), DNMT3A (P= 0.019) and ASXL1 (P= 0.146). More patients treated with imetelstat vs. placebo had ≥50% VAF reduction in these mutations.

For patients with the SF3B1 mutation, 29.5% (23/78) of those treated with imetelstat vs. 2.6% (1/38) on placebo (P=0.001) had a ≥50% VAF reduction. Imetelstat treatment resulted in sustained reduction of SF3B1 VAF over time. In the imetelstat group, 83% (19/23) of patients had 8-week TI among patients who achieved ≥50% maximum reduction from baseline in SF3B1 VAF vs. 38% (21/55) of those who did not.

Similarly, TI responders were also enriched in imetelstat-treated patients achieving ≥50% reduction in TET2 VAF. In the imetelstat group, 83% (10/12) of patients had 8-week RBC-TI among patients who achieved ≥50% maximum

reduction from baseline in TET2 VAF vs 43% (10/23) of those who did not.

In imetelstat-treated patients, 24-week and 1-year TI responders were enriched in patients achieving ≥50% reduction in SF3B1 and TET2 VAF. VAF reduction in SF3B1, TET2 and DNMT3A correlated with longer TI duration and increases in hemoglobin levels in imetelstat-treated patients. Further, 8-week and 24-week TI correlated with reduction in RS+ cells, cytogenetic responses and VAF reduction. These correlations suggest the disease-modifying activity of imetelstat.

Presentation Title: Analysis of Patient-Reported Fatigue in IMerge Phase 3 Trial of Imetelstat vs. Placebo in Heavily Transfused Non-Del(5q) Lower Risk Myelodysplastic Syndromes Relapsed/Refractory to Erythropoiesis Stimulating Agents (ESA)

“The patient-reported outcome data from IMerge Phase 3 is particularly important as fatigue is a concern for lower risk MDS patients, most of whom are elderly. Furthermore, many of the current treatments for these patients cause fatigue. It is therefore very welcome news that imetelstat-treated patients showed sustained meaningful improvement in patient-reported fatigue vs. placebo. This is the first Phase 3 trial we know of to show an improvement in fatigue in lower risk MDS patients,” stated Dr. Platzbecker.

The EHA presentation described results from an exploratory analysis from IMerge Phase 3 of patient-reported fatigue conducted using Functional Assessment of Chronic Illness Therapy, or FACIT, a validated 13-item patient questionnaire. The analysis reported imetelstat-treated patients were more likely to have sustained meaningful improvement in fatigue, as well as experience such improvement more quickly.

Patients treated with imetelstat reported a lower rate of sustained meaningful deterioration in fatigue than placebo (43.2% vs 45.6%), while also receiving fewer transfusion units over time. For patients treated with imetelstat, there was a numerically higher percentage of patients reporting any episode of sustained meaningful improvement in fatigue. Further, patients receiving imetelstat experienced a shorter median time to first sustained clinically meaningful improvement in fatigue vs placebo (28.3 vs 65.0 weeks).

For patients treated with imetelstat, there were significant associations between sustained meaningful improvement in fatigue and 8- and 24-week TI and HI-E response rates, an association not seen in the placebo group.

Additional analysis showed that patients experiencing grade 3 or 4 neutropenia or thrombocytopenia had the same rates of sustained meaningful improvement in fatigue (52.5% and 53.4%, respectively) as the total imetelstat population (50%).

Additional Presentations at EHA

In addition to these IMerge Phase 3 presentations, Geron collaborators presented a translational analysis from a subset of IMerge Phase 2 patients, as well as imetelstat myelofibrosis (MF) pre-clinical results.

The presentation slides and posters are available on the Publications section of Geron's website: **https://www.geron.com/research-and-development/publications/**.

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 TI). Key secondary endpoints include the rate of RBC-TI lasting at least 24 weeks (24-week TI), the duration of 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 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 MF whose disease has relapsed after or is refractory to janus associated kinase (JAK) inhibitor treatment. Geron plans to submit a New Drug Application (NDA) in the U.S. in June 2023 and a Marketing Authorization Application (MAA) in the EU in the second half of 2023 in the lower risk MDS indication.

About Geron

Geron is a late-stage biopharmaceutical company pursuing therapies with the potential to extend and enrich the lives of patients living with hematologic malignancies. Our first-in-class telomerase inhibitor, imetelstat, harnesses Nobel Prize-winning science in a treatment that may alter the underlying drivers of disease. Geron currently has two Phase 3 pivotal clinical trials underway evaluating imetelstat in lower risk myelodysplastic syndromes (LR MDS), and 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, those regarding: (i) that for IMerge Phase 3, Geron plans to submit a New Drug Application in the U.S. in June 2023 and a Marketing Authorization Application in the EU in the second half of 2023; (ii) a potential U.S. commercial launch of imetelstat for lower risk MDS in the first half of 2024; (iii) that imetelstat may alter the underlying biology of lower risk MDS and has the potential to demonstrate disease-modifying activity in patients; and (iv) 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 the current or evolving effects of the COVID-19 pandemic and/or geopolitical events and resulting global economic and financial disruptions will materially and adversely impact Geron's business and business prospects, its financial condition and the future of imetelstat; (b) whether Geron overcomes all of the potential delays and other adverse impacts caused by the current or evolving effects of the COVID-19 pandemic and/or geopolitical events, as well as all the enrollment, clinical, safety, efficacy, technical, scientific, intellectual property, manufacturing and regulatory challenges in order to have the financial resources for, and to meet the expected timelines, planned milestones and expenses; (c) whether regulatory authorities permit the further development of imetelstat on a timely basis, or at all, without any clinical holds; (d) whether imetelstat has demonstrated sufficient safety, efficacy and clinical benefit in IMerge Phase 3 to enable regulatory approval; (e) whether any future safety or efficacy results cause the benefit-risk profile of imetelstat to become unacceptable; (f) whether imetelstat actually demonstrates that it alters the underlying biology of lower risk MDS and has disease-modifying activity in patients;; (g) that Geron may seek to raise substantial additional capital in order to complete the development and commercialization of imetelstat to meet the expected timelines, planned milestones and expenses; (h) whether there are failures or delays in manufacturing or supplying sufficient quantities of imetelstat or other clinical trial materials that impact a commercial launch in lower risk MDS; (i) whether the follow-up period of 12 months for the IMerge Phase 3 primary analysis was sufficient to demonstrate

safety and efficacy, including transfusion independence and clinical benefit, and obtain regulatory approval; and (j) for IMerge Phase 3, the FDA may require Geron to submit additional information or require advisory committee procedures that could cause a regulatory approval, if any, to be delayed. 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 March 31, 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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