Geron Announces Positive Top-Line Results from IMerge Phase 3 Trial of Imetelstat in Lower Risk MDS

- *Trial met primary 8-week transfusion independence (TI) endpoint and key secondary 24-week TI endpoint with highly statistically significant and clinically meaningful improvements*
- *Median TI duration approaching one year for imetelstat 8-week TI responders and 1.5 years for imetelstat 24-week TI responders*
- *Statistically significant and clinically meaningful efficacy results achieved across key MDS subtypes, including ring sideroblast (RS+/RS-) status, high and very high transfusion burden and Low and Intermediate-1 IPSS risk categories*
- *Safety results consistent with prior imetelstat clinical experience with no new safety signals*
- *Clinical and molecular evidence support the potential for MDS disease modification*
- *Request for rolling submission of U.S. New Drug Application (NDA) granted and 2023 plans on target for regulatory submissions in the U.S. and EU*
- *Conference call with Geron management scheduled at 8 a.m. ET this morning*

FOSTER CITY, Calif., January 4, 2023 – Geron Corporation (Nasdaq: GERN), a late-stage clinical biopharmaceutical company, today announced positive top-line results from its IMerge Phase 3 clinical trial evaluating the Company's first-in-class telomerase inhibitor, imetelstat, in lower risk myelodysplastic syndromes (MDS) patients who are relapsed, refractory or ineligible for erythropoiesis stimulating agents (ESAs). The trial met its primary efficacy endpoint of 8-week TI and a key secondary endpoint of 24-week TI, demonstrating highly statistically significant and clinically meaningful benefit of imetelstat versus placebo with no new safety signals and safety results consistent with prior imetelstat clinical trials.

"Today is a great day for lower risk MDS patients who are living with the burden of transfusions. The results from the IMerge Phase 3 study were resoundingly positive, presenting compelling durability of transfusion independence, delivering on the promise of imetelstat and telomerase inhibition for these patients," said John A. Scarlett, M.D., Geron's Chairman and Chief Executive Officer. "This milestone is the first of many upcoming catalysts for Geron, with planned U.S. and EU regulatory submissions in 2023, as well as preparations for a potential U.S. commercial launch. In addition, in 2024, we expect an interim analysis of the IMpactMF Phase 3 trial of imetelstat in relapsed/refractory myelofibrosis."

Summary of Top-Line Results: Primary 8-Week TI Endpoint and Key 24-Week TI Secondary Endpoint Met with Statistical Significance and Meaningful Clinical Improvements

Significant and durable transfusion independence achieved with imetelstat versus placebo

IMerge Phase 3 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, ESA treatment, had not received prior treatment with either a hypomethylating agent (HMA) or lenalidomide and were non-del(5q).

The table below summarizes the top-line efficacy results from the primary analysis of data from IMerge Phase 3, which showed a highly statistically significant and clinically meaningful difference between imetelstat and the placebo comparator arm for the primary endpoint of 8-week TI and key secondary endpoint of 24-week TI. With a

clinical data cut-off occurring in October 2022, median time on study and median time on treatment for patients on imetelstat was approximately 20 months and 8 months, respectively, and approximately 18 months and 7 months for placebo, respectively.

	Imetelstat (n=118)	Placebo (n=60)	P-value*
8-week TI, n (%)	**47 (39.8)**	**9 (15.0)**	**<0.001**
95% confidence interval	(30.9, 49.3)	(7.1, 26.6)	
24-week TI, n (%)	**33 (28.0)**	**2 (3.3)**	**<0.001**
95% confidence interval	(20.1, 37.0)	(0.4, 11.5)	

* Cochran Mantel Haenszel test stratified for prior RBC transfusion burden (≤6 units or >6 units of RBCs/8 weeks) and baseline IPSS risk score (Low or Intermediate-1)

Highly statistically significant (p<0.001; hazard ratio 0.23) durable transfusion independence for 8-week TI responders was achieved with a median TI duration approaching one year for imetelstat, compared to approximately 13 weeks for placebo, using Kaplan-Meier estimates. The median TI duration was approximately 1.5 years (80 weeks) for imetelstat 24-week TI responders.

Transfusion independence achieved broadly across lower risk MDS subtypes

As shown in the table below, statistically significant (p<0.05) 8-week TI was demonstrated with imetelstat versus placebo across lower risk MDS subtypes, including RS+ and RS- status, high and very high transfusion burden and IPSS Low and Intermediate-1 risk status, with similar 8-week TI responses seen for imetelstat within each subtype category.

8-Week TI	Imetelstat, n (%)	Placebo, n (%)	Difference (95% CI)	P-value*
Overall	47/118 (39.8)	9/60 (15.0)	24.8 (9.9, 36.9)	**<0.001**
WHO category				
RS+	33/73 (45.2)	7/37 (18.9)	26.3 (5.9, 42.2)	**0.016**
RS-	14/44 (31.8)	2/23 (8.7)	23.1 (-1.3, 40.6)	**0.038**
Transfusion burden				
4-6 units	28/62 (45.2)	7/33 (21.2)	23.9 (1.9, 41.4)	**0.027**
>6 units	19/56 (33.9)	2/27 (7.4)	26.5 (4.7, 41.8)	**0.023**
IPSS risk category				
Low	32/80 (40.0)	8/39 (20.5)	19.5 (-0.1, 35.2)	**0.034**
Intermediate-1	15/38 (39.5)	1/21 (4.8)	34.7 (8.8, 52.4)	**0.004**

* Cochran Mantel Haenszel test stratified for prior RBC transfusion burden (≤6 units or >6 units of RBCs/8 weeks) and baseline IPSS risk score (Low or Intermediate-1)

Increase in hemoglobin levels, reduction in RBC transfusions and hematologic improvement-erythroid (HI-E)

Mean hemoglobin levels in imetelstat patients increased significantly (p<0.001) over time compared to placebo patients. For patients achieving 8-week TI, median increases in hemoglobin were 3.6 g/dL for imetelstat and 0.8 g/dL for placebo. Imetelstat patients also experienced a statistically significant (p=0.042) and clinically meaningful mean reduction in RBC transfusion units compared to placebo.

A highly statistically significant (p<0.001) HI-E rate was achieved for imetelstat (42.4%) versus placebo (13.3%) using the IWG 2018 criteria for HI-E. The original IMerge protocol was finalized in 2015, and applying the IWG 2006 HI-E criteria in use at that time, the difference between the imetelstat and placebo patients was not statistically

significant (p=0.112). The current IWG 2018 HI-E criteria places greater emphasis on durability by measuring response for ≥16 weeks, rather than ≥8 weeks as specified by the IWG 2006 criteria.

Clinical and molecular evidence supporting the potential for MDS disease modification with imetelstat

Clinical and molecular evidence supporting the potential for MDS disease modification with imetelstat included a one-year median TI duration for imetelstat 8-week TI responders, a median rise of 3.6 g/dL in hemoglobin levels in those same patients and ≥50% variant allele frequency decreases in SF3B1, TET2, DNMT3A and ASXL1 mutations.

"The notable results from IMerge Phase 3 underscore our belief that, with the unique mechanism of action of imetelstat as a telomerase inhibitor, the drug has the potential to become a first-in-class therapy for lower risk MDS patients. The meaningful clinical results observed in the trial, including duration of TI, increases in hemoglobin levels, decreases in transfusions and reductions in mutation burdens, suggest imetelstat treatment may be altering the course of the disease. We look forward to presenting additional data from the trial at medical meetings later this year to further develop the evidence for potential disease modification previously observed in Phase 2 trials in both lower risk MDS and relapsed/refractory MF," said Faye Feller, M.D., Chief Medical Officer of Geron. "I would also like to express my deep appreciation to the Geron employees, past and present, as well as all of the patients and their families, the clinicians, study coordinators and site personnel, whose participation in this trial was integral to obtaining the results we are presenting today."

Safety results consistent with prior clinical experience with imetelstat

The treatment emergent adverse events (TEAEs) observed in IMerge Phase 3 were consistent with the known safety profile of imetelstat from prior clinical trials and no new safety signals were found. Overall treatment discontinuation rates were consistent between the imetelstat and placebo groups (77.1% vs. 76.3%, respectively). Treatment discontinuation rates related to lack of efficacy were higher for the placebo group (42.4%) versus imetelstat (23.7%), and lower for adverse events between the placebo and imetelstat groups (0.0% vs. 16.1%, respectively).

The most common non-hematologic TEAEs (≥10%) in the imetelstat group included asthenia, COVID-19, peripheral edema, headache, diarrhea and alanine aminotransferase increase. Grade 3 liver function test (LFT) elevations reported in the trial were transient and reversible to Grade 2 or lower, with no cases of liver test elevations consistent with Hy's Law or Drug-Induced Liver Injury observed.

The most frequent hematologic TEAEs were Grade 3/4 thrombocytopenia (61.9% imetelstat vs. 8.5% placebo) and neutropenia (67.8% imetelstat vs. 3.4% placebo). Clinical consequences from cytopenias, such as >Grade 3 bleeding events, infections and febrile neutropenia, were similar between the imetelstat and placebo groups. Furthermore, the median duration was shorter for imetelstat for thrombocytopenia (1.4 weeks for imetelstat vs. 2.0 weeks for placebo) and for neutropenia (1.9 weeks for imetelstat vs. 2.2 weeks for placebo). In addition, resolution of Grade 3/4 cytopenias to Grade 2 or lower by laboratory assessment within four weeks was higher for imetelstat, both for thrombocytopenia (86.3% for imetelstat vs. 44.4% for placebo) and neutropenia (81.0% for imetelstat vs. 50.0% for placebo).

"The IMerge Phase 3 efficacy results illustrate the depth, breadth and durability of transfusion independence potentially achievable with imetelstat treatment, which could be practice changing, if approved. These results are especially encouraging, because today we have limited treatment options for lower risk MDS patients that provide broad and durable transfusion independence," said Uwe Platzbecker, M.D., a principal investigator of IMerge Phase 3. "With regards to the safety results, cytopenias were manageable and reversible. Importantly for hematologists, who are accustomed to managing cytopenias, clinical consequences were limited and similar to placebo treated patients. As a once per month out-patient IV therapy, imetelstat will hopefully become a novel treatment option for lower risk MDS patients in the near future."

Planned Next Steps

In light of the positive top-line results from IMerge Phase 3, combined with data from earlier clinical trials, the Company plans to submit an NDA in the U.S. in mid-2023 and a Marketing Authorization Application (MAA) in the EU in the second half of 2023. With Fast Track designation for imetelstat from the U.S. Food and Drug Administration for 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 ESA, a request for rolling submission of the NDA was submitted and has been granted.

Geron also plans to present additional data from IMerge Phase 3 at medical meetings later this year, including data relating to potential correlations of decreases in mutation burden and abnormal cytogenetic clones with clinical responses, patient reported outcomes, hTERT and telomerase activity biomarker data and continued follow-up of durability of transfusion independence, that may be indicative of the potential for disease modification with imetelstat.

Geron is preparing for an anticipated commercial launch of imetelstat in lower risk MDS in the first half of 2024 in the U.S. and by the end of 2024 in the EU, assuming regulatory approvals are granted.

Conference Call Details

A presentation of the data described in this press release is available on the Events and Presentations section (https://ir.geron.com/investors/events) of Geron's website. A conference call with Geron management to review the IMerge Phase 3 top-line results is scheduled at 8 a.m. Eastern Time this morning and may be accessed on Geron's website.

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 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 defined 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.

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. The Company's investigational 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 a Phase 3 clinical trial underway evaluating imetelstat in each of: (i) lower risk myelodysplastic syndromes (LR MDS), and (ii) 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 imetelstat in lower risk MDS, Geron plans to submit an NDA in the U.S. in mid-2023 and an MAA in the EU in the second half of 2023, and is preparing for an anticipated commercial launch in the U.S. in the first half of 2024 and in the EU in the second half of 2024; (ii) that for IMpactMF, Geron expects to conduct an interim analysis in 2024; (iii) that IMerge Phase 3 and IMpactMF have registrational intent; (iv) that imetelstat has the potential for MDS disease modification; (v) that imetelstat has the potential to become a first-in-class therapy for lower risk MDS patients; (vi) that the IMerge Phase 3 efficacy results illustrate the depth, breadth and durability of transfusion independence potentially achievable with imetelstat treatment, which could be practice changing if approved; 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 regulatory authorities determine that imetelstat in lower risk MDS is sufficiently safe and efficacious and grant regulatory approval; (c) whether regulatory authorities accept for filing Geron's planned NDA and MAA submissions; (d) whether any past or future efficacy or safety results may cause the benefit-risk profile of imetelstat to become unacceptable; (e) whether imetelstat actually demonstrates disease-modifying activity in patients in clinical trials; (f) whether regulatory authorities require additional clinical testing of imetelstat prior to granting any approval in lower risk MDS even though IMerge Phase 3 met its primary endpoint; (g) whether there are failures in manufacturing or supplying sufficient quantities of imetelstat that delay, or do not permit, the anticipated commercial launches in (i) above; (h) for IMpactMF, Geron's projected rates for enrollment and death events may differ from actual rates, which may cause the interim analysis to occur later than 2024; (i) whether Geron is able to enroll IMpactMF at a pace that would enable the financial resources for and meet the expected timeline for the interim analysis in 2024; and (j) whether Geron may decide to partner and not to commercialize independently in the U.S. or EU. 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, 2022, 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.

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