Geron Announces First Patient Dosed in IMproveMF Phase 1 Combination Study in Frontline Myelofibrosis

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- Preclinical data showed synergistic and additive effects of combination imetelstat and ruxolitinib
- Study intended to explore potential for disease modification with imetelstat in earlier, frontline myelofibrosis setting
- Single-agent imetelstat currently being studied in a separate Phase 3 trial designed to confirm clinically meaningful benefits observed in relapsed/refractory MF patients in Phase 2 study

FOSTER CITY, Calif.--(BUSINESS WIRE)-- Geron Corporation (Nasdaq: GERN), a late-stage clinical biopharmaceutical company, today announced that the first patient has been dosed in IMproveMF, a Phase 1 study evaluating imetelstat, a first-in-class telomerase inhibitor, in combination with ruxolitinib in patients with frontline myelofibrosis (MF).

“We designed the Phase 1 IMproveMF study based on preclinical data that showed the sequential treatment of ruxolitinib followed by imetelstat had a selective inhibitory effect on malignant MF stem cells, while sparing normal hematopoietic stem cells. This disease-modifying potential of imetelstat to affect the malignant clones driving disease progression differentiates it from any other drug currently approved or in development for myelofibrosis treatment,” said Faye Feller, MD, Executive Vice President, Chief Medical Officer of Geron. “Given these preclinical data, we want to explore the potential for disease modification with imetelstat in the earlier, frontline disease setting. In parallel, our separate IMpactMF Phase 3 trial is ongoing in MF patients who are relapsed/refractory to JAK inhibitors. This Phase 3 trial is designed to confirm the results from the IMbark Phase 2 study where single-agent imetelstat treatment resulted in multiple clinically meaningful benefits, including symptom response and potential improvement in overall survival.”

“Upon diagnosis, intermediate-2 and high-risk myelofibrosis patients typically receive ruxolitinib as the primary therapy, which reduces enlarged spleens and alleviates symptoms, but does not change the course of the disease. As a non-JAK inhibitor treatment option with a potentially novel mechanism of action, imetelstat could provide an additive benefit of disease modification when combined with ruxolitinib,” said John Mascarenhas, MD, Professor of Medicine at the Icahn School of Medicine at Mount Sinai and a principal investigator on the IMproveMF study. “The

dosing of the first patient is an important step in identifying a potential safe and efficacious dose and schedule of imetelstat and ruxolitinib in frontline MF."

IMproveMF is a single arm, open label, two-part Phase 1 study to evaluate the safety, pharmacokinetics, pharmacodynamics and clinical activity of imetelstat in combination with ruxolitinib as a frontline treatment in patients with Intermediate-2 or High-risk MF (frontline MF). In both parts, patients will receive ruxolitinib followed by imetelstat, a dosing schedule that showed synergistic and additive effects of the two drugs in preclinical experiments. Part 1 will enroll up to 20 frontline MF patients who, at the time of enrollment, have received an optimized dose of ruxolitinib, to which imetelstat treatment will be added at increasing dose levels based on safety and tolerability. The primary purpose of Part 1 is to identify a safe dose for treating frontline MF patients with a combination of imetelstat and ruxolitinib. If a safe dose is identified in Part 1, participants in Part 2 will be JAK inhibitor naïve and will receive treatment with ruxolitinib after screening and enrollment at a starting dose based on standard-of-care or local prescribing information. Treatment with single-agent ruxolitinib will continue for at least 12 weeks, including four consecutive weeks at a stable dose prior to the addition of imetelstat. Part 2 is designed to confirm the safety profile of imetelstat in combination with ruxolitinib and to evaluate for preliminary clinical activity of the combination. Geron expects to present preliminary results from this study by the end of 2023.

The study is enrolling patients and is being conducted at three trial sites in the U.S., two of which are currently open for patient screening. For more information, please visit **ClinicalTrials.gov** (Identifier NCT05371964).

About Imetelstat

Imetelstat is a novel, first-in-class telomerase inhibitor exclusively owned by Geron and being developed in hematologic malignancies. Data from Phase 2 clinical trials 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 United States Food and Drug Administration for both the treatment of patients with non-del(5q) lower risk MDS who are refractory or resistant to an erythropoiesis stimulating agent and for 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 clinical biopharmaceutical company focused on the development and potential commercialization of a first-in-class telomerase inhibitor, imetelstat, in hematologic malignancies. The Company currently is conducting two Phase 3 clinical trials: IMerge in lower risk myelodysplastic syndromes and IMpactMF in refractory myelofibrosis.

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 imetelstat has disease-modifying potential to affect the malignant clones driving disease progression; (ii) that IMproveMF is intended to explore the potential for disease modification with imetelstat in earlier, frontline myelofibrosis setting; (iii) that with a potentially novel mechanism of action, imetelstat could provide an additive benefit of disease modification when combined with ruxolitinib; (iv) that there could be a potential safe and efficacious dose and schedule of imetelstat and ruxolitinib in frontline MF; (v) that IMproveMF Part 1 will enroll up to 20 frontline MF patients and may potentially identify a safe dose for treating frontline MF patients with a combination of imetelstat and ruxolitinib; (vi) that Geron expects to present preliminary results from IMproveMF by the end of 2023; (vii) 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; and (viii) 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 the Russia/Ukraine conflict cause global economic and financial disruptions that 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 the Russia/Ukraine conflict, and overcomes 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 timeline of the end of 2023 for the preliminary results from IMproveMF; (c) whether regulatory authorities permit the further development of imetelstat on a timely basis, or at all, without any clinical holds; (d) whether any 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 and the ability to target the malignant stem and progenitor cells of the underlying disease; (f) whether there are failures or delays in manufacturing or supplying sufficient quantities of imetelstat or other clinical trial materials in a timely manner, or at all; (g) whether Geron can accurately project the timing of enrollment in IMproveMF, whether due to the current or evolving effects of the COVID-19 pandemic, the Russia/Ukraine conflict, or otherwise; (h) and whether imetelstat combined with ruxolitinib demonstrates that it is safe and effective in patients with frontline MF. 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 June 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 to reflect future information, events or circumstances.

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