Geron Announces Plans for Imetelstat Phase 3 Clinical Trial in Myelofibrosis and Other Updates

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- Geron plans to move forward with a Phase 3 clinical trial in refractory myelofibrosis (MF) with overall survival (OS) as a primary endpoint, which is expected to open for screening and enrollment in first quarter 2021
- Completion of patient enrollment for the ongoing IMerge Phase 3 clinical trial in lower risk myelodysplastic syndromes (MDS) is expected first quarter 2021
- Revised operating expense guidance of $70 - $75 million for 2020
- Conference call scheduled for Thursday, May 28 at 4:30 p.m. ET

MENLO PARK, Calif., May 21, 2020 (GLOBE NEWSWIRE) -- Geron Corporation (Nasdaq: GERN), a late-stage clinical biopharmaceutical company, today announced plans for a Phase 3 clinical trial in MF patients who are refractory to treatment with a janus kinase (JAK) inhibitor, including trial design and expected timelines for trial start and future data readouts. Geron also provided an update on its ongoing IMerge Phase 3 clinical trial in lower risk MDS and reported revised fiscal year 2020 operating expense guidance.

“We are very pleased to announce that following a productive meeting with the FDA, we plan to move forward with a randomized Phase 3 clinical trial in refractory MF,” said John A. Scarlett, M.D., Chairman and Chief Executive Officer. “Our planned Phase 3 clinical trial in refractory MF will compare imetelstat to best available therapy that excludes JAK inhibitors and has overall survival as the primary endpoint. Also, we have an ongoing Phase 3 clinical trial in lower risk MDS with transfusion independence as the primary endpoint and durability of transfusion independence as a key secondary endpoint. We believe the results from these two Phase 3 clinical trials will differentiate imetelstat, due to its unique mechanism of action, from currently available therapies and enable Geron to become a leader in the treatment of hematologic myeloid malignancies.”

Planned Phase 3 Clinical Trial in Refractory Myelofibrosis (MF)

The planned Phase 3 clinical trial in refractory MF is designed to be an open label 2:1 randomized, controlled trial to

evaluate imetelstat (9.4 mg/kg administered by intravenous infusion every three weeks) in approximately 320 patients with Intermediate-2 or High-risk MF. Patients eligible for the trial will be required to be refractory to a JAK inhibitor, an inclusion criterion that is planned to be defined as having an inadequate spleen response or symptom response after treatment with a JAK inhibitor for at least six months, including an optimal dose of a JAK inhibitor for at least two months. The control arm is planned to be best available therapy (BAT), excluding JAK inhibitors. The primary efficacy endpoint for the trial is planned to be overall survival (OS). Planned key secondary endpoints include symptom response, spleen response, progression free survival, complete response, partial response, clinical improvement, duration of response, safety, pharmacokinetics, and patient reported outcomes.

Currently, the planned Phase 3 clinical trial in refractory MF has been designed with more than 85% power to detect a 40% reduction in the risk of death for the imetelstat treated patients (hazard ratio=0.60; one-sided alpha=0.025), for example, 14 months for the BAT arm and 23 months for the imetelstat arm. The final analysis for OS is planned to be conducted after more than 50% of the total enrolled patients have died. An interim analysis of OS, in which the alpha spend is expected to be approximately 0.01, is planned to be conducted after approximately 70% of the total projected number of events, or deaths, for the final analysis have occurred. At the interim analysis, if the pre-specified statistical OS criterion is met, then Geron expects such data may support registration of imetelstat in refractory MF. If the prespecified OS criterion is not met at interim analysis, the trial will continue to the final analysis. Both the planned interim and final analyses are event driven and could occur on different timelines than currently expected.

The trial design for the planned Phase 3 clinical trial in refractory MF was discussed with the U.S. Food and Drug Administration (FDA) at a Type C meeting in the second quarter of 2020. The FDA accepted the proposed trial design, including the definition of the refractory MF patient population, the primary efficacy endpoint of OS, secondary endpoints, the use of BAT for the control arm that excludes JAK inhibitors, and the statistical design and methods to be used to analyze data from the trial for the interim and final analyses. Although the FDA urged Geron to consider a third dosing arm to assess a lower dose and/or a more frequent dosing schedule that might identify a less toxic regimen and/or improve spleen response, one of the trial's secondary endpoints, the FDA did not object to Geron's proposed imetelstat dose and schedule of 9.4 mg/kg every three weeks. Geron believes the current design of the planned Phase 3 clinical trial will support, if the trial is successful, the registration of imetelstat in refractory MF.

Currently, Geron expects to engage over 150 sites to participate in the global Phase 3 clinical trial in refractory MF across North America, South America, Europe and Asia. Geron plans to open the trial for screening and enrollment in the first quarter of 2021. Under current assumptions, Geron expects to complete patient enrollment in the planned Phase 3 clinical trial in refractory MF in the second half of 2022, to conduct an interim analysis in the first half of 2023 and to conduct a final analysis in the first half of 2024. The timing and achievement of enrollment

completion and either or both of the planned analyses depend on numerous factors, including obtaining regulatory clearance of the trial protocol, Geron's ability to raise additional capital, and delays or interruptions related to the evolving effects of the COVID-19 pandemic.

Update on IMerge Phase 3 Clinical Trial in Lower Risk Myelodysplastic Syndromes (MDS)

As of the end of April 2020, approximately 68% of planned clinical sites for the IMerge Phase 3 clinical trial in lower risk MDS were open for enrollment. Due to the effects of the COVID-19 pandemic on site initiations and enrollment, Geron now plans to complete patient enrollment by the end of the first quarter of 2021. To facilitate this timing, the Company is currently evaluating the feasibility of increasing the number of participating countries by six, and the number of clinical sites by 40. Following 15 months from the last patient being enrolled, a primary analysis of efficacy and safety data from the trial will begin to enable top-line results. Under current assumptions, the Company expects top-line results to be available in the second half of 2022. This anticipated timing is subject to potential delays or interruptions associated with the evolving effects of the COVID-19 pandemic, regardless of Geron's evaluation of additional countries and sites.

The IMerge Phase 3 clinical trial has been designed with more than 85% power to detect a statistically significant difference in the primary endpoint of 8-week transfusion independence between the imetelstat treatment arm and the placebo arm. Based on discussions with U.S. and European regulatory authorities, Geron believes the IMerge Phase 3 clinical trial, if successful, will support the registration of imetelstat in lower risk MDS.

Revised Guidance and Development Priorities

The Company expects its 2020 operating expense burn to range from $70 to $75 million. This guidance reflects cash conservation measures implemented in April due to the COVID-19 pandemic, such as suspending travel and postponing a planned imetelstat proof of concept study, as well as the new costs for startup activities associated with the planned Phase 3 clinical trial in refractory MF and the additional costs for the expansion of clinical sites for the IMerge Phase 3 clinical trial. Spending in 2020 is expected to support the following development priorities, subject to the evolving effects of the COVID-19 pandemic:

Development priorities for 2020

- Startup activities for the planned Phase 3 clinical trial in refractory MF to enable the trial to be open for screening and enrollment in the first quarter of 2021.

- Continue working with investigators participating in the ongoing IMerge Phase 3 clinical trial in order to complete patient enrollment in the trial by the end of the first quarter of 2021.

- Oral presentation of more mature IMerge Phase 2 data, including durability of transfusion independence in lower risk MDS, at the Virtual European Hematology Association (EHA) Annual Congress on June 12.

  An abstract published online on May 14, 2020 described long-term efficacy and safety data, including one-year transfusion free interval and the longest median duration of red blood cell transfusion independence reported to date in the trial. The abstract is available on the EHA website at **www.ehaweb.org/congress**.

- Poster presentations at the Virtual EHA Annual Congress of new analyses from IMbark Phase 2 data providing further evidence of observed improvement in OS as an indicator of potential disease-modifying activity of imetelstat in relapsed/refractory MF.

  Three abstracts published online on May 14, 2020 suggest that dose-related improvements in OS correlate with other clinical benefits, such as symptom and spleen response as well as fibrosis improvement observed in the trial; improvements in OS in a patient subpopulation with a poor prognosis due to the absence of the three primary driver mutations in MF, or triple-negative; and dose-dependent inhibition of telomerase with imetelstat, resulting in on-target activity that correlates with improvement in OS. Taken together, Geron believes the three MF abstracts substantiate the OS outcome observed in IMbark and support the planned Phase 3 clinical trial in refractory MF.

The previously announced proof of concept study in High-risk MDS and acute myeloid leukemia (AML), originally expected to begin in the fourth quarter of 2020, has been postponed in order to prioritize the Phase 3 clinical trials in lower risk MDS and refractory MF.

Upcoming Events

- Q1 2020 Financial Results May 28, after market close
- Virtual Annual Stockholder Meeting June 5, 8 a.m. PT
- Virtual EHA Annual Congress June 11-14
- Post-EHA KOL Virtual Event June 17, before market open

Conference Call

Geron will host a conference call at 4:30 p.m. ET on Thursday, May 28, 2020 to discuss plans for the Phase 3 clinical trial in refractory MF, as well as an update on the IMerge Phase 3 clinical trial and first quarter financial results.

Participants may access the conference call live via telephone by dialing domestically +1 (833) 513-0551 or internationally +1 (647) 689-4209. The conference ID is 5582655. A live, listen-only webcast will also be available on the Company's website at **www.geron.com/investors/events**. If you are unable to listen to the live call, an archived webcast will be available on the Company's website for 30 days.

Unmet Medical Need in Lower Risk Myelodysplastic Syndromes (MDS)

MDS is a group of blood disorders in which the continuous upregulation of telomerase is associated with the proliferation of malignant progenitor cells which produces multiple malignant cell clones in the bone marrow resulting in disordered and ineffective production of the myeloid lineage, which includes red blood cells, white blood cells and platelets. In MDS, bone marrow and peripheral blood cells may have abnormal, or dysplastic, cell morphology. MDS is frequently characterized clinically by severe anemia, or low red blood cell counts, and low hemoglobin. In addition, other peripheral cytopenias, or low numbers of white blood cells and platelets, may cause life-threatening infections and bleeding. Transformation to AML occurs in up to 30% of MDS cases and results in poorer overall survival.

MDS is the most common of the myeloid malignancies and is primarily a disease of the elderly, with median age at diagnosis around 70 years. In addition, MDS patients are grouped using the World Health Organization (WHO) classification system, which was most recently updated in 2016. It divides MDS into types based mainly on how the cells in the bone marrow look under the microscope, as well as other factors. Common MDS subgroups include ringed sideroblast positive, or RS+, and ringed sideroblast negative, or RS-.

The majority of MDS patients, approximately 70%, fall into what are considered to be the lower risk groups at diagnosis, according to the International Prognostic Scoring System that takes into account the presence of a number of disease factors, such as cytopenias and cytogenetics, to assign relative risk of progression to AML and overall survival. There are more than 100,000 people worldwide and 40,000 people in the U.S. living with lower risk MDS. In addition, more than 10,000 new cases of lower risk MDS are reported each year in the U.S. Based on Geron's internal estimates of pricing and addressable patient population, if imetelstat is approved for commercial use by the FDA and foreign regulatory authorities in lower risk MDS, Geron believes the annual revenue potential in lower risk MDS in the U.S. could exceed $500 million and $1 billion worldwide.

Chronic anemia is the predominant clinical problem in patients who have lower risk MDS. Many of these patients become dependent on red blood cell transfusions due to low hemoglobin. Serial red blood cell transfusions can lead to elevated levels of iron in the blood and other tissues, which the body has no normal way to eliminate. Iron

overload is a potentially dangerous condition. Studies in patients with MDS have shown that iron overload resulting from regular red blood cell transfusions is associated with a poorer overall survival and a higher risk of developing AML.

Geron believes that imetelstat, a first-in-class telomerase inhibitor, has the potential to inhibit the uncontrolled proliferation of malignant stem and progenitor cells in MDS, resulting in reduction of dysfunctional blood cell production and potentially enabling recovery of normal hematopoiesis.

Unmet Medical Need in Intermediate-2 or High-risk Myelofibrosis (MF)

MF, a type of myeloproliferative neoplasm, is a chronic blood cancer in which abnormal or malignant precursor cells in the bone marrow proliferate rapidly, causing scar tissue, or fibrosis, to form. As a result, normal blood production in the bone marrow is impaired and may shift to other organs, such as the spleen and liver, which can cause them to enlarge. People with MF may have abnormally low or high numbers of circulating red blood cells, white blood cells or platelets, and abnormally high numbers of immature cells in the blood or bone marrow. MF patients can also suffer from debilitating constitutional symptoms, such as drenching night sweats, fatigue, severe itching, or pruritus, abdominal pain, fever and bone pain.

Approximately 70% of MF patients are classified as having Intermediate-2 or High-risk disease, as defined by the Dynamic International Prognostic Scoring System Plus described in a 2011 Journal of Clinical Oncology article. There are more than 35,000 patients worldwide and more than 13,000 patients in the U.S. living with Intermediate-2 or High-risk MF. In addition, more than 2,000 new cases are reported each year in the U.S. Based on Geron's internal estimates of pricing and addressable patient population, if imetelstat is approved for commercial use by the FDA and foreign regulatory authorities in refractory MF, Geron believes the annual revenue potential in refractory MF in the U.S. could exceed $750 million and $1.5 billion worldwide.

The only drug therapies approved by the FDA for treating MF patients with Intermediate-2 or High-risk disease are the JAK inhibitors, ruxolitinib and fedratinib. According to medical literature, approximately 50% of patients discontinue treatment with ruxolitinib within three years and 75% within five years due to disease progression, adverse events, and unsatisfactory response to treatment. Currently, no drug therapy is specifically approved by the FDA for those patients who fail or no longer respond to JAK inhibitor treatment, and median survival for such refractory MF patients after discontinuation from ruxolitinib is only approximately 14 to 16 months, representing a significant unmet medical need.

As a telomerase inhibitor, Geron believes that imetelstat has the potential to inhibit the uncontrolled proliferation of malignant stem and progenitor cells in refractory MF patients to reduce dysfunctional blood cell production and potentially enable recovery of normal hematopoiesis.

About Imetelstat

Imetelstat is a novel, first-in-class telomerase inhibitor exclusively owned by Geron and being developed in hematologic myeloid malignancies. Early clinical data suggest imetelstat may have disease-modifying activity through the apoptosis of malignant stem and progenitor cells, which allows potential recovery of normal hematopoiesis. Geron's imetelstat development program includes two ongoing or planned registration-enabling studies, IMerge, an ongoing Phase 2/3 clinical trial in lower risk myelodysplastic syndromes (MDS), and a planned Phase 3 clinical trial in refractory myelofibrosis (MF) expected to be open for patient screening and enrollment in the first quarter of 2021. Imetelstat has been granted Fast Track designation by the U.S. 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 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 myeloid malignancies. For more information about Geron, visit **www.geron.com**.

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) the therapeutic potential of imetelstat, including imetelstat's potential survival benefit for refractory MF patients; (ii) that for the planned Phase 3 clinical trial in refractory MF, Geron expects to begin patient enrollment in the first quarter of 2021, complete patient enrollment in the second half of 2022, conduct an interim analysis in the first half of 2023 and conduct a final analysis in the first half of 2024; (iii) the design, commencement and conduct of the planned Phase 3 clinical trial in refractory MF; (iv) that imetelstat may have disease-modifying activity; (v) that for IMerge, Geron expects to complete enrollment in the first quarter of 2021 and have top-line results in the second half of 2022; (vi) IMerge's design, including that IMerge will potentially demonstrate durable transfusion independence; (vii) that the combined potential revenue for imetelstat in lower risk MDS and refractory MF could exceed $1.25 billion in the U.S. and $2.5 billion worldwide; (viii) Geron's development priorities for 2020; (ix) that Geron's 2020 operating expense range will be $70-75 million; and (x) 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 evolving effects of the COVID-19 pandemic 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 evolving effects of the COVID-19 pandemic, and overcomes the clinical, safety, efficacy, technical, scientific, intellectual property, manufacturing and regulatory challenges in order to meet the expected timelines and planned milestones in (ii), (v) and (viii) above; (c) whether regulatory authorities permit the further development of imetelstat on a timely basis, or at all, without any clinical holds; (d) whether imetelstat is demonstrated to be safe and efficacious in clinical trials; (e) whether any future efficacy or safety results may cause the benefit-risk profile of imetelstat to become unacceptable; (f) whether imetelstat actually demonstrates disease-modifying activity in patients; (g) that Geron may not successfully market imetelstat or that competition could cause imetelstat not to achieve the revenue potential in (vii) above; (h) whether imetelstat is able to maintain patent protection, obtain and maintain the orphan drug exclusivity and have freedom to operate; (i) Geron's need to raise substantial capital in order to complete the development and commercialization of imetelstat, including to meet all of the expected timelines and planned milestones in (ii), (v) and (viii) above; (j) whether there are cost overruns in 2020 due to the evolving effects of the COVID-19 pandemic or otherwise; (k) whether Geron can accurately project or attain complete enrollment in IMerge, the planned Phase 3 refractory MF trial or of any potential future clinical trials of imetelstat, whether due to the evolving effects of the COVID-19 pandemic or otherwise; and (l) whether there are failures or delays in manufacturing sufficient quantities of imetelstat or other clinical trial materials in a timely manner, whether due to the evolving effects of the COVID-19 pandemic or otherwise. 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 Annual Report on Form 10-K for the year ended December 31, 2019, Geron's Current Report on Form 8-K filed on May 8, 2020, and future filings and reports by Geron, including Geron's preliminary prospectus supplement to be filed with the SEC on or about the date hereof. 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.

CONTACT:

Suzanne Messere
Investor and Media Relations
investor@geron.com
media@geron.com

CG Capital
877-889-1972

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