CTI BioPharma Announces FDA Accelerated Approval of VONJO™ (pacritinib) for the Treatment of Adult Patients with Myelofibrosis and Thrombocytopenia

March 1, 2022

- VONJO is the First Approved Therapy to Specifically Address the Needs of Adult Cytopenic Myelofibrosis Patients -
- NDA Approved Under Priority Review -
- Approval Triggers $60 Million Payment from DRI Healthcare Trust -
- CTI to Host Conference Call Tomorrow at 8:00 a.m. ET -

SEATTLE, Feb. 28, 2022 /PRNewswire/ -- CTI BioPharma Corp. (Nasdaq: CTIC) today announced the U.S. Food and Drug Administration (FDA) has approved VONJO (pacritinib) for the treatment of adults with intermediate or high-risk primary or secondary (post-polycythemia vera or post-essential thrombocythemia) myelofibrosis with a platelet count below 50×10^9/L. VONJO is a novel oral kinase inhibitor with specificity for JAK2 and IRAK1, without inhibiting JAK1. The recommended dosage of VONJO is 200 mg orally twice daily. VONJO is the first approved therapy that specifically addresses the needs of patients with cytopenic myelofibrosis.

"Today's approval of VONJO establishes a new standard of care for myelofibrosis patients suffering from cytopenic myelofibrosis," said John Mascarenhas, M.D., Associate Professor, Medicine, Hematology and Medical Oncology, Tisch Cancer Institute, Icahn School of Medicine at Mount Sinai, New York. "Myelofibrosis with severe thrombocytopenia, defined as blood platelet counts below 50×10^9/L, has been shown to result in poor survival outcomes coupled with debilitating symptoms. Limited treatment options have rendered this disease as an area of urgent unmet medical need. I am pleased to see that a new, efficacious and safe treatment option is now available for these patients."

"In the U.S., there are approximately 21,000 patients with myelofibrosis, two-thirds of which have cytopenias (thrombocytopenia or anemia), commonly resulting from the toxicity of other approved therapies. Severe thrombocytopenia, defined as a blood platelet count below 50×10^9/L, occurs in one-third of the overall myelofibrosis population, and has a particularly poor prognosis. With the approval of VONJO, we are excited to now be able to offer a new therapy that is specifically approved for patients with cytopenic myelofibrosis. We are fully funded for commercial launch, following our debt and royalty transactions with DRI, and we look forward to providing VONJO, the potential best-in-class therapy for cytopenic myelofibrosis patients, to patients within 10 days," said Adam R. Craig, M.D., Ph.D., President and Chief Executive Officer of CTI Biopharma. "I would like to thank the patients, caregivers, clinical trial staff and investigators who made the VONJO clinical trials possible. I am also thankful to the CTI team for their hard work and dedication and their focus on the needs of patients."

The accelerated approval is based on efficacy results from the pivotal Phase 3 PERSIST-2 study of VONJO in patients with myelofibrosis (platelet counts less than or equal to 100×10^9/L). Patients were randomized 1:1:1 to receive VONJO 200 mg twice daily (BID), VONJO 400 mg once daily (QD) or best available therapy (BAT). Prior JAK2 inhibitor therapy was permitted. In this study, in the cohort of patients with baseline platelet counts below 50×10^9/L who were treated with pacritinib 200 mg BD, 29% of patients had a reduction in spleen volume of at least 35% compared to 3% of patients receiving best available therapy, which included ruxolitinib. As part of the accelerated approval, CTI is required to describe a clinical benefit in a confirmatory trial. To fulfil this post-approval requirement, CTI plans to complete the PACIFICA trial, with expected results in mid-2025.

The most common adverse reactions (≥20%) following VONJO 200 mg twice daily were diarrhea, thrombocytopenia, nausea, anemia and peripheral edema. The most frequent serious adverse reactions (≥3%) following VONJO 200 mg twice daily were anemia, thrombocytopenia, pneumonia, cardiac failure, disease progression, pyrexia and squamous cell carcinoma of skin.

CTI is committed to supporting patients with myelofibrosis and removing barriers to access. As part of that commitment, CTI has established CTI Access, a patient support program that provides reimbursement and financial assistance programs for eligible patients. For more information, visit www.CTIaccess.com.

Under the terms of the previously announced debt and royalty transaction with DRI Healthcare Trust, the FDA approval of VONJO triggers the acquisition by DRI of a tiered royalty on VONJO for US$60 million. The proceeds of the transactions will be used by CTI to fund the launch of VONJO. As of December 31, 2021, CTI had cash and cash equivalents of approximately $65 million.

Conference Call and Webcast
CTI will host a conference call and webcast to discuss this announcement tomorrow, March 1, at 8:00 a.m. ET. To access the live call by phone please dial (877) 735-2860 (domestic) or (602) 563-8791 (international); the conference ID is 8860186. A live audio webcast of the event may also be accessed through the "Investors" section of CTI's website at www.ctibiopharma.com. A replay of the webcast will be available for 30 days following the event.

About VONJO (pacritinib)
Pacritinib is an oral kinase inhibitor with activity against wild type Janus Associated Kinase 2 (JAK2), mutant $JAK2^{V617F}$ form and FMS-like tyrosine kinase 3 (FLT3), which contribute to signaling of a number of cytokines and growth factors that are important for hematopoiesis and immune function. Myelofibrosis is often associated with dysregulated JAK2 signaling. Pacritinib has higher inhibitory activity for JAK2 over other family members, JAK3 and TYK2. At clinically relevant concentrations, pacritinib does not inhibit JAK1. Pacritinib exhibits inhibitory activity against additional cellular kinases (such as CSF1R and IRAK1), the clinical relevance of which is unknown.

VONJO is indicated for the treatment of adults with intermediate or high-risk primary or secondary (post-polycythemia vera or post-essential

thrombocythemia) myelofibrosis with a platelet count below 50 × 10^9/L. This indication is approved under accelerated approval based on spleen volume reduction. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).

Important VONJO Safety Information

Hemorrhage:

Serious (11%) and fatal (2%) hemorrhages have occurred in VONJO-treated patients with platelet counts <100 × 10^9/L. Serious (13%) and fatal (2%) hemorrhages have occurred in VONJO-treated patients with platelet counts <50 × 10^9/L. Grade ≥3 bleeding events (defined as requiring transfusion or invasive intervention) occurred in 15% of patients treated with VONJO compared to 7% of patients treated on the control arm. Due to hemorrhage, VONJO dose-reductions, dose interruptions, or permanent discontinuations occurred in 3%, 3%, and 5% of patients, respectively.

Avoid use of VONJO in patients with active bleeding and hold VONJO 7 days prior to any planned surgical or invasive procedures. Assess platelet counts periodically, as clinically indicated. Manage hemorrhage using treatment interruption and medical intervention.

Diarrhea:

VONJO causes diarrhea in approximately 48% of patients compared to 15% of patients treated on the control arm. The median time to resolution in VONJO-treated patients was 2 weeks. The incidence of reported diarrhea decreased over time with 41% of patients reporting diarrhea in the first 8 weeks of treatment, 15% in Weeks 8 through 16, and 8% in Weeks 16 through 24. Diarrhea resulted in treatment interruption in 3% of VONJO-treated patients. None of the VONJO-treated patients reported diarrhea that resulted in treatment discontinuation. Serious diarrhea adverse reactions occurred in 2% of patients treated with VONJO compared to no such adverse reactions in patients in the control arm.

Control pre-existing diarrhea before starting VONJO treatment. Manage diarrhea with antidiarrheal medications, fluid replacement, and dose-modification. Treat diarrhea with anti–diarrheal medications promptly at the first onset of symptoms. Interrupt or reduce VONJO dose in patients with significant diarrhea despite optimal supportive care.

Thrombocytopenia:

VONJO can cause worsening thrombocytopenia. VONJO dosing was reduced due to worsening thrombocytopenia in 2% of patients with pre–existing moderate to severe thrombocytopenia (platelet count <100 × 10^9/L). VONJO dosing was reduced due to worsening thrombocytopenia in 2% of patients with pre–existing severe thrombocytopenia (platelet count <50 × 10^9/L).

Monitor platelet count prior to VONJO treatment and as clinically indicated during treatment. Interrupt VONJO in patients with clinically significant worsening of thrombocytopenia that lasts for more than 7 days. Restart VONJO at 50% of the last given dose once the toxicity has resolved. If toxicity recurs hold VONJO. Restart VONJO at 50% of the last given dose once the toxicity has resolved.

Prolonged QT interval:

VONJO can cause prolongation of the QTc interval. QTc prolongation of >500 msec was higher in VONJO-treated patients than in patients in the control arm (1.4% vs 1%). QTc increase from baseline by 60 msec or higher was greater in VONJO-treated patients than in control arm patients (1.9% vs 1%). Adverse reactions of QTc prolongation were reported for 3.8% of VONJO-treated patients and 2% of control arm patients. No cases of torsades de pointes were reported.

Avoid use of VONJO in patients with a baseline QTc of >480 msec. Avoid use of drugs with significant potential for QTc prolongation in combination with VONJO. Correct hypokalemia prior to and during VONJO treatment. Manage QTc prolongation using VONJO interruption and electrolyte management.

Major Adverse Cardiac Events (MACE):

Another Janus associated kinase (JAK)-inhibitor has increased the risk of MACE, including cardiovascular death, myocardial infarction, and stroke (compared to those treated with TNF blockers) in patients with rheumatoid arthritis, a condition for which VONJO is not indicated.

Consider the benefits and risks for the individual patient prior to initiating or continuing therapy with VONJO particularly in patients who are current or past smokers and patients with other cardiovascular risk factors. Patients should be informed about the symptoms of serious cardiovascular events and the steps to take if they occur.

Thrombosis:

Another JAK-inhibitor has increased the risk of thrombosis, including deep venous thrombosis, pulmonary embolism, and arterial thrombosis (compared to those treated with TNF blockers) in patients with rheumatoid arthritis, a condition for which VONJO is not indicated.

Patients with symptoms of thrombosis should be promptly evaluated and treated appropriately.

Secondary Malignancies:

Another JAK-inhibitor has increased the risk of lymphoma and other malignancies excluding non-melanoma skin cancer (NMSC) (compared to those treated with TNF blockers) in patients with rheumatoid arthritis, a condition for which VONJO is not indicated. Patients who are current or past smokers are at additional increased risk.

Consider the benefits and risks for the individual patient prior to initiating or continuing therapy with VONJO, particularly in patients with a known malignancy (other than a successfully treated NMSC), patients who develop a malignancy, and patients who are current or past smokers.

Risk of Infection:

Another JAK-inhibitor has increased the risk of serious infections (compared to best available therapy) in patients with myeloproliferative neoplasms. Serious bacterial, mycobacterial, fungal and viral infections may occur in patients treated with VONJO. Delay starting therapy with VONJO until active serious infections have resolved. Observe patients receiving VONJO for signs and symptoms of infection and manage promptly. Use active surveillance and prophylactic antibiotics according to clinical guidelines.

Interactions with CYP3A4 Inhibitors or Inducers:

Co-administration of VONJO with strong CYP3A4 inhibitors or inducers is contraindicated. Avoid concomitant use of VONJO with moderate CYP3A4 inhibitors or inducers.

Drug interruptions due to an adverse reaction occurred in 27% patients who received VONJO 200 mg twice daily compared to 10% of patients treated with BAT. Dosage reductions due to an adverse reaction occurred in 12% of patients who received VONJO 200 mg twice daily compared to 7% of patients treated with BAT. Permanent discontinuation due to an adverse reaction occurred in 15% of patients receiving VONJO 200 mg twice daily compared to 12% of patients treated with BAT.

Please visit http://www.ctibiopharma.com/vonjo_prescribing_information for full Prescribing Information and the Medication Guide.

To report Adverse Events or Product Quality Complaints, contact CTI BioPharma Corp, at 1-844-428-4246 (844-4CTIBIO) or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

About Myelofibrosis
Myelofibrosis is bone marrow cancer that results in formation of fibrous scar tissue and can lead to thrombocytopenia and anemia, weakness, fatigue and an enlarged spleen and liver. Within the U.S., there are approximately 21,000 patients with myelofibrosis, 7,000 of which have severe thrombocytopenia (defined as blood platelet counts below 50×10^9/L). Severe thrombocytopenia is associated with poor survival and high symptom burden and can occur as a result of disease progression or from drug toxicity with other JAK2 inhibitors, such as JAKAFI and INREBIC.

About CTI BioPharma Corp.
We are a commercial biopharmaceutical company focused on the acquisition, development and commercialization of novel targeted therapies for blood-related cancers that offer a unique benefit to patients and their healthcare providers. CTI has one FDA-approved product VONJO™ (pacritinib), a JAK2 and IRAK1, that spares JAK1. VONJO is approved for the treatment of adults with intermediate or high-risk primary or secondary (post-polycythemia vera or post-essential thrombocythemia) myelofibrosis with a platelet count below 50×10^9/L. CTI is conducting the Phase 3 PACIFICA study of VONJO in patients with myelofibrosis and severe thrombocytopenia as a post-marketing requirement.

VONJO™ is a trademark of CTI BioPharma Corp.

Cautionary Note Regarding Forward-Looking Statements
Statements included in this press release that are not historical in nature are forward-looking statements within the meaning of Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934 and the Private Securities Litigation Reform Act of 1995. These forward-looking statements are based on current assumptions that involve risks, uncertainties and other factors that may cause the actual results, events or developments to be materially different from those expressed or implied by such forward-looking statements. These risks and uncertainties include, but are not limited to: our ability to successfully commercialize VONJO; our ability to conduct and complete clinical trials in our currently anticipated timeframes; our expectations regarding the completion and outcome of our PACIFICA Phase 3 trial, including the risk that the FDA may determine that the benefit/risk profile of pacritinib does not support the continued approval of VONJO; the accuracy of our assumptions regarding our planned expenditures and sufficiency of our cash to fund operations; and the commercial launch of VONJO; risks and uncertainties related to the COVID-19 pandemic as it relates to our operations and ongoing clinical trials; and those risks more fully discussed in the section entitled "Risk Factors" in our Annual Report on Form 10-K for the year ended December 31, 2020 and subsequent quarterly reports on Form 10-Q. These forward-looking statements speak only as of the date hereof and we assume no obligation to update these forward-looking statements, and readers are cautioned not to place undue reliance on such forward-looking statements. "CTI BioPharma" and the CTI BioPharma logo are registered trademarks or trademarks of CTI BioPharma Corp. in various jurisdictions. All other trademarks belong to their respective owner.

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