Terns Pharmaceuticals Announces Global Phase 1 Clinical Trial Design of TERN-701 for the Treatment of Chronic Myeloid Leukemia

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Investigational New Drug application cleared by U.S. Food and Drug Administration

Design leverages insights from partner's ongoing Phase 1 trial in China that support starting dose that appears safe and clinically active based on emerging early clinical data

Patient screening anticipated in December 2023, with initial data expected in second half of 2024

FOSTER CITY, Calif., Oct. 16, 2023 (GLOBE NEWSWIRE) -- Terns Pharmaceuticals, Inc. ("Terns" or the "Company") (Nasdaq: TERN), a clinical-stage biopharmaceutical company developing a portfolio of small-molecule product candidates to address serious diseases, including oncology, non-alcoholic steatohepatitis (NASH) and obesity, today announced the U.S. Food and Drug Administration's (FDA's) clearance of the Company's Investigational New Drug application and the design of the CARDINAL Trial, Terns' global Phase 1 clinical trial to evaluate the safety, tolerability, pharmacokinetics (PK) and efficacy of TERN-701 in participants with chronic myeloid leukemia (CML). TERN-701 is the Company's proprietary, allosteric BCR-ABL tyrosine kinase inhibitor (TKI), designed to target the BCR-ABL myristoyl pocket.

"Allosteric BCR-ABL inhibitors comprise a novel class of therapy for CML that has been shown to have superior efficacy and improved safety compared to active-site inhibitors in prior studies. We are particularly pleased with our Phase 1 trial design for TERN-701 as it will recruit chronic CML patients who experienced treatment failure on at least one prior second-generation TKI. This will allow us to offer a novel investigational allosteric inhibitor to CML patients in as early as their second line of therapy, where there are currently no approved allosteric inhibitors," said Emil Kuriakose, MD, chief medical officer-oncology at Terns Pharmaceuticals.

"Importantly, we were able to leverage emerging early clinical data from the ongoing Phase 1 trial in China conducted by our partner, Hansoh, to inform the dose selection for the CARDINAL Trial. This enables us to accelerate our study and the overall development of this molecule, while enhancing our ability to best dose optimize TERN-701 for patients with CML."

"We are excited to continue the clinical development momentum of TERN-701, which we believe can offer a valuable alternative to the only FDA-approved allosteric BCR-ABL TKI for CML. We are well-positioned to report initial data from this global Phase 1 trial in the second half of 2024," continued Dr. Kuriakose.

Phase 1 CARDINAL Trial Design
The CARDINAL Trial is a global, multicenter, open-label, two-part Phase 1 clinical trial to evaluate the safety, PK, and efficacy of TERN-701 in participants with previously treated CML. Part 1 is the dose escalation portion of the trial that will evaluate once-daily TERN-701 monotherapy in approximately 24-36 adults living with CML to be enrolled in up to five dose cohorts. Participants will have chronic phase CML with confirmed BCR-ABL and a history of treatment failure or suboptimal response to at least one second generation TKI (nilotinib, dasatinib or bosutinib). Participants who are intolerant to prior TKI treatment (including asciminib) are also allowed. The primary endpoints for Part 1 are the incidence of dose limiting toxicities (DLTs) during the first treatment cycle, and additional measures of safety and tolerability. Secondary endpoints include TERN-701 PK and efficacy assessments, such as hematologic and molecular responses as measured by the change from baseline in BCR-ABL transcript levels. The starting dose is 160 mg QD (once-daily) with dose escalations as high as 500 mg QD and the option to explore a lower dose of 80 mg QD.

Part 2 is the dose expansion portion of the trial that will enroll approximately 40 patients, randomized to once-daily treatment with one of two doses of TERN-701 to be selected based on data from Part 1. The primary endpoint of the dose expansion portion of the trial is efficacy, measured by hematologic and molecular responses. Secondary endpoints include safety, tolerability and PK. The overall objective of the CARDINAL Trial is to select the optimal dose(s) of TERN-701 to move forward to a potential pivotal trial in chronic phase CML.

The CARDINAL Trial plans to enroll at sites in the U.S., Europe and other Terns global territories. Global site identification and trial start-up activities are ongoing, with the first patient screening expected in December 2023. More information about the TERN-701 global Phase 1 (CARDINAL Trial) trial may be found on clinicaltrials.gov when available.

About TERN-701
TERN-701 is Terns' proprietary, oral, potent, allosteric BCR-ABL TKI specifically targeting the BCR-ABL myristoyl pocket, which is in clinical development for chronic myeloid leukemia. Allosteric TKIs, which bind to the myristoyl-binding pocket, represent a novel treatment class for CML and have the potential to address the shortcomings of active-site TKIs, including off-target activity and limited efficacy against active site resistance mutations. TERN-701 aims to address the limitations of active-site TKIs with the goal

of achieving improved tumor suppression through a combination of potent activity against BCR-ABL including a broad range of mutations and improved safety and tolerability profiles. Terns anticipates initiation of the CARDINAL Trial, a global Phase 1 trial for TERN-701, in the second half of 2023, with potential interim top-line readouts from initial cohorts in 2024. Hansoh's Phase 1 trial (NCT05367700) evaluating the tolerability, efficacy, and pharmacokinetics of once-daily TERN-701 (HS-10382) for CML in China is ongoing.

About Chronic Myeloid Leukemia
CML is a cancer that occurs when the blood-forming cells of the bone marrow overproduce white blood cells. In the United States, CML is an orphan indication with approximately 8,930 new cases expected to be diagnosed in 2023. As of 2020, the latest year for which statistics are available, an estimated 66,366 people are either living with or in remission from CML.[i] Since the introduction of tyrosine kinase inhibitor (TKI) therapy in 2001, CML has been transformed from a life-threatening disease to a life-long chronic condition for most patients. Despite improvements in outcomes with active-site targeting TKIs, many patients do not achieve long-term disease control with these therapies due to resistance or intolerance, leading patients to cycle through prior generation treatments. As a result, physicians and patients are seeking additional efficacious therapies for people whose tolerability, co-morbidity and/or drug-drug interaction profiles change over time, limiting their available treatment options, quality of life and the effectiveness of mainstay therapies. Allosteric BCR-ABL TKIs are the only class of drug to show efficacy and tolerability benefits over active-site TKIs, and represent an important advancement in the treatment of CML.

About Terns Pharmaceuticals
Terns Pharmaceuticals, Inc. is a clinical-stage biopharmaceutical company developing a portfolio of small-molecule product candidates to address serious diseases, including oncology, NASH and obesity. Terns' pipeline includes two clinical stage development programs including an allosteric BCR-ABL inhibitor and a THR-β agonist, and preclinical small-molecule GLP-1 receptor agonist and GIPR modulator programs. For more information, please visit: www.ternspharma.com.

Cautionary Note Regarding Forward-Looking Statements
This press release contains forward-looking statements about Terns Pharmaceuticals, Inc. (the "Company," "we," "us," or "our") within the meaning of the federal securities laws, including those related to the Company's expectations of timing and potential results of the clinical trials and other development activities of the Company and its partners, including timelines related to the TERN-701 Phase 1 trial; the potential indications to be targeted by the Company with its small-molecule product candidates; the therapeutic potential of the Company's small-molecule product candidates, including the potential for its product candidates such as TERN-701 to be safe and efficacious; the potential for the mechanisms of action of the Company's product candidates to be therapeutic targets for their targeted indications; the potential utility and progress of the Company's product candidates in their targeted indications, including the clinical utility of the data from and the endpoints used in the Company's and its partner's clinical trials; the Company's clinical development plans and activities, including the results of any interactions with regulatory authorities on its programs; the Company's expectations regarding the profile of its product candidates, including efficacy, tolerability, safety, metabolic stability and pharmacokinetic profile and potential differentiation as compared to other products or product candidates; the Company's plans for and ability to continue to execute on its current development strategy, including potential combinations involving multiple product candidates; and the impact of new legislation and regulatory developments on the Company's plans for its product candidates, such as the effect of the Inflation Reduction Act of 2022. All statements other than statements of historical facts contained in this press release, including statements regarding the Company's strategy, future financial condition, future operations, future trial results, projected costs, prospects, plans, objectives of management and expected market growth, are forward-looking statements. In some cases, you can identify forward-looking statements by terminology such as "aim," "anticipate," "assume," "believe," "contemplate," "continue," "could," "design," "due," "estimate," "expect," "goal," "intend," "may," "objective," "plan," "positioned," "potential," "predict," "seek," "should," "target," "will," "would" and other similar expressions that are predictions of or indicate future events and future trends, or the negative of these terms or other comparable terminology. The Company has based these forward-looking statements largely on its current expectations, estimates, forecasts and projections about future events and financial trends that it believes may affect its financial condition, results of operations, business strategy and financial needs. In light of the significant uncertainties in these forward-looking statements, you should not rely upon forward-looking statements as predictions of future events. These statements are subject to risks and uncertainties that could cause the actual results and the implementation of the Company's plans to vary materially, including the risks associated with the initiation, cost, timing, progress, results and utility of the Company's current and future research and development activities and preclinical studies and clinical trials. These risks are not exhaustive. For a detailed discussion of the risk factors that could affect the Company's actual results, please refer to the risk factors identified in the Company's SEC reports, including but not limited to its Annual Report on Form 10-K for the year ended December 31, 2022. Except as required by law, the Company undertakes no obligation to update publicly any forward-looking statements for any reason.

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[i] Arber DA, Orazi A, Hasserjian RP, et al. International consensus classification of myeloid neoplasms and acute leukemias: integrating morphologic, clinical, and genomic data. Blood. 2022:140(11);1200-1228