Terns Pharmaceuticals Announces Positive Early Data from Phase 1 CARDINAL Trial of TERN-701 for Chronic Myeloid Leukemia

December 3, 2024

Compelling molecular responses starting at lowest dose level in heavily pre-treated patients with high baseline BCR-ABL transcript levels

Encouraging safety profile with no dose limiting toxicities, adverse event-related treatment discontinuations, or dose reductions across three dose escalation cohorts

High levels of target coverage achieved with once daily dosing at all doses

Completion of dose escalation and initiation of dose expansion expected in 1H25

Additional efficacy data expected in 4Q25, including longer term major molecular response (MMR) rates

Company to host webcast at 8:00 am ET today

FOSTER CITY, Calif., Dec. 03, 2024 (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 and obesity, today announced encouraging early data from the ongoing dose escalation part of the Phase 1 CARDINAL study evaluating TERN-701 in patients with relapsed/refractory chronic myeloid leukemia (CML).

TERN-701 is an investigational, oral, potent, small molecule allosteric BCR-ABL inhibitor being developed for patients with CML. CARDINAL is a global, multicenter, open-label, two-part Phase 1 clinical trial to evaluate the safety, pharmacokinetics (PK), and efficacy of TERN-701 in patients with relapsed/refractory CML with or without BCR-ABL resistance mutations who were previously treated with at least one 2G tyrosine kinase inhibitor (TKI). Patients previously treated with asciminib are also eligible.

“These exciting early data from our Phase 1 dose escalation cohorts clearly show TERN-701 has compelling clinical activity with a highly encouraging cumulative MMR rate of 50% at 3 months. At the first two dose levels, we see clinically meaningful molecular and hematologic responses in patients with high baseline BCR-ABL transcript levels who had poor responses on prior 2G TKIs, 3G TKIs including ponatinib, as well as asciminib,” said Emil Kuriakose MD, chief medical officer of Terns.

“The emerging safety data show a profile supporting best-in-class potential with no dose limiting toxicities across three completed dose levels, no clinically meaningful changes in liver or pancreatic enzymes, and no AE-related dose reductions or discontinuations at doses that achieve plasma exposures well above target efficacious concentrations. Taken together, the clinical activity and safety data across the dose range in these heavily pre-treated patients with refractory disease support a potential wide therapeutic index that allows for high levels of target coverage with favorable safety/tolerability.”

“We are thrilled to share these impactful early data from the Phase 1 CARDINAL study of TERN-701, which support its potential to be a best-in-class allosteric inhibitor for the treatment of CML,” said Amy Burroughs, chief executive officer of Terns. “In addition to the meaningful clinical data, the CARDINAL study highlights yet another example of excellent clinical and operational execution at Terns, with patients enrolled in all four dose escalation cohorts in less than a year. We are well-positioned to initiate dose expansion cohorts in the first half of 2025 and look forward to sharing additional safety and efficacy data, including longer term MMR data in late 2025.”

As of the October 28, 2024 cutoff date, 15 patients were enrolled across three dose levels of 160mg (n=7), 320mg (n=5), and 400mg (n=3) of TERN-701 dosed once daily, with an overall median treatment duration of 3 months (range 0.79 - 7.5 months). Enrolled patients were heavily pretreated with a median of 4 prior TKIs (range: 1-6) and 80% having had 3 or more TKIs. 47% and 40% of patients, respectively, had previously received ponatinib and asciminib. 73% were not in MMR at baseline, with 60% having a baseline BCR-ABL transcript >1% international scale (IS). As of the data cutoff, 14 of 15 patients remain on treatment.

Twelve patients were efficacy evaluable, defined as having baseline BCR-ABL transcript and at least two post-baseline BCR-ABL transcript levels (centrally assessed). All efficacy evaluable patients were in the 160mg and 320mg dose levels. Key efficacy highlights include:

- 88% (7/8) of patients with baseline transcript > 1% had decreases in BCR-ABL on treatment, with 7 ongoing as of data cutoff
- Cumulative MMR rate of 50% (5/10) in non-T315i mutation patients with 3 or more months of treatment and/or MMR or better at baseline
- 100% (4/4) of patients with MMR or better at baseline have maintained their response and remain on treatment
- Additional notable responses include:
    - MR2 within 5 months in a 4L patient at 160mg QD with baseline transcript > 1% and suboptimal response and intolerance to asciminib
    - MR4 (deep molecular response) within 3 months in a 5L patient treated at 320mg with baseline transcript >10% and treatment failure on bosutinib at study entry

TERN-701 showed a highly encouraging safety profile across the 160mg to 400mg dose levels, with 500mg undergoing evaluation as of data cutoff. Key safety highlights:

- No dose limiting toxicities (DLT) through 400mg dose level
- No adverse event (AE)-related treatment discontinuations or dose reductions
- No Grade 3 or higher treatment-related AEs
- No treatment related serious AEs

The incidence of treatment emergent hematologic AEs was notably low in this heavily pre-treated population, with no Grade 3 or higher treatment-related cytopenias. There were no non-hematologic treatment-related AEs more than Grade 2 in severity. Finally, no clinically meaningful changes in liver and pancreatic enzymes, blood pressure and other vitals, or electrocardiogram were seen.

Steady state PK data, available for the 160mg and 320mg dose levels at data cutoff, showed linear PK with dose proportional increases in exposure. Plasma protein binding-corrected $C_{average}$ for TERN-701 exceeded the in vitro IC90 for multiple mutated and non-mutated BCR-ABL variants with once daily dosing. Importantly, at 160mg and 320mg QD, TERN-701 achieved average free drug concentrations approximately 4-fold and 8-fold higher, respectively, than *in vivo* exposures where potent inhibition of the BCR-ABL signaling pathway in was seen in CML mouse tumor models, indicating robust pharmacodynamic effects at these clinical doses.

As of December 3, 2024, the CARDINAL study has enrolled 19 patients inclusive of the 500mg cohort, with all dose escalation cohorts having enrolled at least 3 patients. The study is on track to initiate dose expansion in the first half of 2025 with additional efficacy data expected in the fourth quarter of 2025, including longer term MMR rates.

Company Webcast
Terns will host a company webcast at 8:00 am ET today. The discussion will cover TERN-701's Phase 1 interim data, next steps for the CARDINAL program, and TERN-701's potential role in the CML treatment landscape.

The event will be webcast live and can be accessed by visiting the investor relations section of the Company's website at https://ir.ternspharma.com. An archived webcast will be available following the event.

About CARDINAL
The CARDINAL trial is an ongoing global, multicenter, open-label, two-part Phase 1 clinical trial to evaluate the safety, PK, and efficacy of TERN-701 in patients with previously treated CML. Part 1 is the dose escalation portion of the trial evaluating once-daily TERN-701 monotherapy in up to five dose cohorts in up to 60 adults with 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 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.

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 and obesity. Terns' pipeline contains three clinical stage development programs including an allosteric BCR-ABL inhibitor, a small-molecule GLP-1 receptor agonist, a THR-β agonist, and a preclinical GIPR modulator discovery effort, prioritizing a GIPR antagonist nomination candidate. For more information, please visit: www.ternspharma.com.

Cautionary Note Regarding Forward-Looking Statements
This press release contains forward-looking statements about the Company within the meaning of the federal securities laws, including those related to expectations, timing and potential results of the clinical trials and other development activities of the Company and its partners; 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; 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 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; the potential commercialization of the Company's product candidates; the Company's plans and expectations around the addition of key personnel; and the Company's expectations with regard to its cash runway and sufficiency of its cash resources. 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, 2023. Except as required by law, the Company undertakes no obligation to update publicly any forward-looking statements for any reason.

Contacts for Terns

Investors
Justin Ng
investors@ternspharma.com

Media
Jenna Urban
Berry & Company Public Relations
media@ternspharma.com