Turning Point Therapeutics Announces Initial Clinical Data From Phase 1/2 SWORD-1 Study of RET Inhibitor TPX-0046

April 5, 2021

- ***Preliminary Clinical Activity Shown, With Tumor Regression in 4 of 5 TKI-Naïve Patients Including 2 Confirmed Partial Responses***
- ***Preliminary Clinical Activity Shown, With Tumor Regression in 3 of 9 TKI-Pretreated Patients***
- ***Across 6 Dose Finding Cohorts, Generally Well Tolerated Preliminary Safety Profile***
- ***Continued Dose Finding with Phase 1 Dose Expansion Planned***
- ***Conference Call Scheduled for 4:30 p.m. Eastern Time***

SAN DIEGO, April 05, 2021 (GLOBE NEWSWIRE) -- Turning Point Therapeutics, Inc. (NASDAQ: TPTX), a precision oncology company developing next-generation therapies that target genetic drivers of cancer, today reported initial clinical data from the ongoing Phase 1/2 SWORD-1 study of its RET inhibitor drug candidate, TPX-0046.

The initial data from the Phase 1 dose finding portion of the study showed preliminary clinical activity, including objective responses and a generally well-tolerated safety profile. Turning Point continues to evaluate doses and schedules to determine a recommended Phase 2 dose, and plans to revise the study protocol to include Phase 1 expansion cohorts at the recommended Phase 2 dose.

“RET-driven cancers affect nearly 10,000 patients annually in the U.S. and E.U., and patients who progress following treatment with a selective RET inhibitor remain particularly underserved,” said Alexander Drilon, M.D., chief, Early Drug Development Service, Memorial Sloan Kettering Cancer Center. “While we continue to evaluate TPX-0046, the initial preliminary data are encouraging, with a generally tolerable safety profile and early signals of activity.”

TPX-0046 Initial Clinical Data
Twenty-one patients enrolled in the study including 10 with non-small cell lung cancer (NSCLC) and 11 with medullary thyroid carcinoma (MTC) who were treated from December 2019 to the data cut-off date of March 10, 2021. Patients included those with RET-altered TKI-naïve NSCLC (n=3; all previously treated with platinum-based chemotherapy and immunotherapy) and MTC (n=2), and TKI-pretreated NSCLC (n=7) and MTC (n=9).

All 16 TKI-pretreated patients were previously treated with a selective RET TKI and 9 patients (56%) were treated with more than 1 prior TKI. Ninety-one percent of patients (19/21) had a baseline ECOG performance score of 1, and nearly half (10/21) received 3 or more prior therapies.

Preliminary efficacy data by investigator assessment was available for 14 evaluable patients with baseline measurable disease and at least one post-baseline assessment per RECIST v1.1, including TKI-naïve NSCLC (n=3) and MTC (n=2), and TKI-pretreated NSCLC (n=4) and MTC (n=5).

As of the March 10, 2021 data cut-off date:

Preliminary Safety and Pharmacokinetic Results

- A total of 21 patients with RET-altered NSCLC or MTC were treated with TPX-0046 across multiple doses and schedules from 10mg once daily (QD) to 30mg QD
- TPX-0046 was generally well tolerated, with the most frequent treatment emergent adverse event (TEAE) being Grade 1 or 2 dizziness
- The maximum tolerated dose had not been determined, with 1 dose-limiting toxicity of treatment-related Grade 2 gait disturbance at 30 mg QD
- TEAEs reported in greater than 20 percent of patients were dizziness (43%); fatigue (38%); alkaline phosphatase increase, constipation, decreased appetite, dry mouth, hyperphosphataemia, lipase increase (29% each); and alanine aminotransferase increase, dehydration, and muscular weakness (24% each)
- There were infrequent dose reductions or drug discontinuations due to TEAEs
- The majority of treatment related adverse events (TRAEs) were Grade 1 or 2 and there were no Grade 4 or 5 TRAEs
- There were no treatment related Grade 3 or greater ALT/AST elevations, any grade of hypertension, hemorrhagic events or QT prolongation, and no interstitial lung disease or pneumonitis
- Preliminary pharmacokinetic data indicates exposure increases in a dose dependent manner

Preliminary Efficacy Results

- Of 5 RET TKI-naïve patients, 4 showed tumor regressions of -42%, -37%, -23%, and -3%, including 2 patients dosed at 30 mg QD who achieved confirmed partial responses with duration of responses of 5.6 and 5.8+ months, respectively. Three of the 4 patients with regressions remained on treatment awaiting their next scan
- Of 9 TKI-pretreated patients, 3 patients (2 treated with only 1 prior selective RET TKI) achieved tumor regressions of -44%, -27% and -17%. All 3 patients remained on treatment awaiting their next scan
- Of the 14 evaluable patients, 7 (50%) remained on treatment with duration of treatment ranging from 5.1 to 51+ weeks

“Given the encouraging data we have seen, we plan to modify the SWORD-1 study to include a dose expansion portion utilizing additional clinical sites,” said Mohammad Hirmand, M.D., executive vice president and chief medical officer of Turning Point Therapeutics. “We look forward to advancing our development of TPX-0046 in both the RET-positive TKI-naïve and less heavily pretreated TKI-pretreated settings.”

After determination of the recommended Phase 2 dose, Turning Point plans to study TPX-0046 in multiple Phase 1 dose expansion cohorts in up to 75 patients with RET-altered malignancies prior to an end of Phase 1 meeting with the Food and Drug Administration.

Webcast and Conference Call
Turning Point will host a webcast and conference call accompanied by a slide presentation to discuss the results at 4:30 p.m. ET today. Athena Countouriotis, M.D., president and chief executive officer, will host the call, which will also include Dr. Hirmand.

The discussion will be accessible through the "Investors" section of tptherapeutics.com or by dialing (877) 388-2118 (in the United States) or (470) 495-9489 (outside the U.S.) using conference ID 9939858. A replay will be available through the "Investors" section of www.tptherapeutics.com.

About Turning Point Therapeutics Inc.
Turning Point Therapeutics is a clinical-stage precision oncology company with a pipeline of internally discovered investigational drugs designed to address key limitations of existing cancer therapies. The company’s lead drug candidate, repotrectinib, is a next-generation kinase inhibitor targeting the ROS1 and TRK oncogenic drivers of non-small cell lung cancer and advanced solid tumors. Repotrectinib, which is being studied in a registrational Phase 2 study in adults and a Phase 1/2 study in pediatric patients, has shown antitumor activity and durable responses among kinase inhibitor treatment-naïve and pre-treated patients. The company’s pipeline of drug candidates also includes TPX-0022, targeting MET, CSF1R and SRC, which is being studied in a Phase 1 trial of patients with advanced or metastatic solid tumors harboring genetic alterations in *MET*; TPX-0046, targeting RET, which is being studied in a Phase 1/2 trial of patients with advanced or metastatic solid tumors harboring genetic alterations in *RET*; and TPX-0131, a next-generation ALK inhibitor. Turning Point’s next-generation kinase inhibitors are designed to bind to their targets with greater precision and affinity than existing therapies, with a novel, compact structure that has demonstrated an ability to potentially overcome treatment resistance common with other kinase inhibitors. The company is driven to develop therapies that mark a turning point for patients in their cancer treatment. For more information, visit www.tptherapeutics.com.

Forward Looking Statements
Statements contained in this press release regarding matters that are not historical facts are “forward-looking statements” within the meaning of the Private Securities Litigation Reform Act of 1995. Such forward-looking statements include statements regarding, among other things, the efficacy, safety and therapeutic potential of TPX-0046, the results, conduct, progress and timing of the Phase 1/2 clinical study of TPX-0046, plans regarding future clinical studies and regulatory discussions, and the regulatory approval path for TPX-0046. Because such statements are subject to risks and uncertainties, actual results may differ materially from those expressed or implied by such forward-looking statements. Words such as “plans”, “will”, “believes,” “anticipates,” “expects,” “intends,” “goal,” “potential” and similar expressions are intended to identify forward-looking statements. These forward-looking statements are based upon Turning Point Therapeutics’ current expectations and involve assumptions that may never materialize or may prove to be incorrect. Actual results could differ materially from those anticipated in such forward-looking statements as a result of various risks and uncertainties, which include, without limitation, risks and uncertainties associated with Turning Point Therapeutics’ business in general, risks and uncertainties related to the impact of the COVID-19 pandemic to Turning Point’s business and the other risks described in Turning Point Therapeutics’ filings with the SEC. All forward-looking statements contained in this press release speak only as of the date on which they were made. Turning Point Therapeutics undertakes no obligation to update such statements to reflect events that occur or circumstances that exist after the date on which they were made.

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