# Turning Point Therapeutics Presents Initial Clinical Data From Phase 1 SHIELD-1 Study of Novel MET/SRC/CSF1R Inhibitor TPX-0022 at 2020 EORTC-NCI-AACR Symposium

October 24, 2020

- ***Preliminary Clinical Activity and Safety Profile Support Advancing to Dose Expansion in Multiple Tumor Types***
- ***Recommended Phase 2 Dose Determination Ongoing***
- ***Preclinical Combination Data for Lead Drug Candidate Repotrectinib in both KRAS Tumor Models and Pediatric Neuroblastoma Tumor Models Also Presented***
- ***Conference Call Scheduled for 11:00 a.m. Eastern Time***

SAN DIEGO, Oct. 24, 2020 (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 dose finding portion of its SHIELD-1 study of drug candidate, TPX-0022, a potent inhibitor of MET and the associated cancer signaling pathways of SRC and CSF1R. The initial data highlighted preliminary clinical activity, including objective responses across multiple tumor types and a generally tolerable safety profile.

The findings were reported in a late-breaking oral presentation by David Hong, M.D., Department of Investigational Cancer Therapeutics, The University of Texas MD Anderson Cancer Center in the plenary session of the Molecular Targets and Cancer Therapeutics virtual symposium hosted by the European Organisation for Research and Treatment of Cancer (EORTC), the National Cancer Institute (NCI) and the American Association for Cancer Research (AACR).

“Oncogenic alterations in MET – including exon 14 deletion, amplifications, fusions and activating kinase domain mutations – occur in many tumor types and patients continue to have limited available therapies,” said Dr. Hong. “The initial data reported today for TPX-0022 is encouraging because it represents the potential for a new targeted therapy to improve the outcome in a wide range of MET-driven cancers.”

**TPX-0022, Phase 1 Initial Clinical Data**
Twenty-two patients were treated across four dose levels from Sept. 2019 to the data cut-off date of Oct. 15, 2020. Patients included those with MET-altered non-small cell lung cancer (n=13), colorectal cancer (n=4), gastric or gastroesophageal (GE) junction cancer (n=4) and glioblastoma (n=1).

The median number of prior therapies was three (range 1 to 6), with all patients having received at least one prior line of chemotherapy and/or immunotherapy and the majority of patients having received multiple rounds of prior combination chemotherapy. Sixty-eight percent of patients had a baseline ECOG performance score of 1.

Preliminary efficacy data was available for 15 evaluable patients with baseline measurable disease and at least one post-baseline scan.

As of the 15 October 2020 data cut-off date:

Preliminary Safety and Pharmacokinetic (PK) Results (n=22)

- A total of 22 patients with MET-dysregulated advanced solid tumors were treated with TPX-0022 at dose levels from 20 mg once daily (QD) to 120 mg QD.
- TPX-0022 was generally well tolerated, with the most frequent treatment emergent adverse event (TEAE) being Grade 1 or 2 dizziness.
- TEAEs reported in greater than 20 percent of patients were dizziness (55%); lipase increased (32%); fatigue (32%); amylase increased (27%); nausea (27%); vomiting (27%); constipation (23%); and anemia (23%).
- The majority of treatment related adverse events (TRAEs) were Grade 1 or 2 and there were no Grade 4 or 5 TRAEs
- The maximum tolerated dose had not been determined, with one dose-limiting toxicity of treatment-related Grade 2 dizziness at 120 mg QD.
- PK data suggested sustained MET inhibition throughout the dosing interval across all doses.

Preliminary Efficacy Results (n=15)

- A total of 15 patients were evaluable for efficacy by investigator assessment, including 10 who were MET TKI-naïve: four with colorectal cancer (CRC), three with non-small cell lung cancer (NSCLC), and three with gastric or GE junction cancer (GC or GEJ). In addition, five patients were MET TKI-pretreated, all with NSCLC.
- Of 10 MET TKI-naïve patients, five achieved a partial response, including three with GC or GEJ cancer, one with CRC, and one with NSCLC. All three evaluable patients with gastric or GEJ tumors achieved a response.

- Of the five responses, three patients achieved a confirmed response, and two patients remained on treatment in a response awaiting confirmation at the time of the data cut-off.
- Of the five MET TKI-pretreated NSCLC patients, three patients treated with multiple rounds of prior therapy achieved a best response of stable disease with two patients showing tumor measurement improvements (-27%, and -75% accordingly).
- Nine of 15 patients (9/15) achieved clinical benefit (confirmed and unconfirmed partial response or stable disease).
- Six of 15 patients (6/15) remained on treatment with duration of treatment ranging from 7.6+ to 34+ weeks.

“We are encouraged by the emerging early safety and efficacy data across multiple tumor types, including the high unmet medical need area within MET-amplified gastric cancer where there are no approved targeted therapies,” said Mohammad Hirmand, M.D., chief medical officer. “MET driven cancers affect a large and growing population of patients who have limited therapeutic options. Based on these early study findings, we look forward to advancing the development of TPX-0022.”

The company anticipates initiating Phase 1 dose expansion after determining the recommended Phase 2 dose. Turning Point plans to discuss the ongoing Phase 1 SHIELD-1 study with the Food and Drug Administration (FDA) to potentially modify the trial into a registrational Phase 1/2 design. The company is targeting initiation of the Phase 2 portion in the second half of 2021, pending FDA feedback. In parallel, based on the SHIELD-1 study initial findings, a combination study with TPX-0022 and an epidermal growth factor receptor (EGFR) tyrosine kinase inhibitor (TKI) in patients with EGFR mutated MET-amplified NSCLC is also planned for initiation in the second half of 2021.

**Repotrectinib Poster Presentations**
In addition, preclinical data for the company’s lead drug candidate repotrectinib were reported in two poster presentations.

The first poster expanded on previous work presented in June at AACR 2020 with additional preclinical data of repotrectinib in combination with the KRAS-G12C inhibitor, AMG-510, in a NSCLC xenograft tumor model. In preclinical studies, repotrectinib significantly enhanced efficacy of AMG-510 and showed a marked survival benefit in a *KRAS* G12C xenograft model when compared to AMG-510 alone.

Repotrectinib previously showed synergy in preclinical models with AMG-510 and inhibited *KRAS* G12C tumor cell proliferation, suppressed receptor tyrosine kinase upregulation induced by AMG-510, and reduced *KRAS* G12C tumor cell cytokine release. Similar results have since been obtained with other *KRAS* G12C inhibitors.

With the new results presented in a *KRAS* G12C xenograft tumor model, and previous data shown with repotrectinib in combination with a MEK inhibitor (presented at AACR 2020), the company now plans to initiate a clinical combination study in KRAS mutant NSCLC in mid-2021. Further details on the design will be shared at the time of study initiation.

The second poster showed preclinical studies of repotrectinib as monotherapy and in combination with irinotecan and temozolomide in neuroblastoma cell lines and pediatric patient-derived xenograft (PDX) models. Repotrectinib combined with chemotherapy demonstrated increased anti-tumor activity compared to chemotherapy alone in an ALK-mutant neuroblastoma PDX model.

“With a growing body of supportive preclinical data, we are encouraged by the potentially broader role for repotrectinib across the treatment landscape,” said Dr. Hirmand. “Repotrectinib’s inhibition of the cancer signaling pathways of SRC, FAK and JAK2, and its generally well-tolerated safety profile make it an ideal candidate for combination therapy. We look forward to advancing our combination strategy toward the initiation of clinical studies in 2021.”

**Webcast and Conference Call**
Turning Point will host a webcast and conference call accompanied by a slide presentation to discuss the results from the SHIELD-1 Phase 1 study of TPX-0022 at 11:00 a.m. ET/8:00 a.m. PT today. Athena Countouriotis, M.D., president and chief executive officer, will host the call, which will also include Dr. Hirmand and Dr. Hong.

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 8655648. 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 called TRIDENT-1 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 in a Phase 1 study called SHIELD-1 in patients with advanced or metastatic solid tumors harboring genetic alterations in *MET*; RET-inhibitor TPX-0046, which is in a Phase 1/2 study of patients with advanced or metastatic solid tumors harboring genetic alterations in *RET*; and ALK-inhibitor TPX-0131, which is in IND-enabling studies. 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-0022 and repotrectinib, the results, conduct, progress and timing of the Phase 1 SHIELD-1 clinical study of TPX-0022, and preclinical studies of repotrectinib, plans regarding future clinical studies and regulatory discussions and the regulatory approval path for TPX-0022. 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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