Turning Point Therapeutics Reports Early Interim Data From Registrational Phase 2 Trident-1 Study of Repotrectinib, Provides Regulatory Update

August 19, 2020

- ***ROS1+ TKI-Naïve Non-Small Cell Lung Cancer Confirmed Objective Response Rate is 86 Percent***
- ***ROS1+ TKI-Pretreated Non-Small Cell Lung Cancer with One Prior TKI and Prior Chemotherapy, Confirmed Objective Response Rate is 40 Percent***
- ***ROS1+ TKI-Pretreated Non-Small Cell Lung Cancer with One Prior TKI without Prior Chemotherapy, Confirmed Objective Response Rate is 67 Percent***
- ***NTRK+ TKI-Pretreated Advanced Solid Tumors Confirmed Objective Response Rate is 50 Percent***
- ***Recent FDA Feedback on TRIDENT-1 Study May Provide Faster Path to Potential Approval***
- ***Conference Call Scheduled for 8:00 a.m. EDT***

SAN DIEGO, Aug. 19, 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 early interim data from the registrational Phase 2 TRIDENT-1 study of lead drug candidate, repotrectinib, and announced recent regulatory feedback from the Food and Drug Administration (FDA) on the TRIDENT-1 trial design.

“We are very encouraged by the early interim data from the Phase 2 TRIDENT-1 study as they reaffirm our belief that repotrectinib has the potential to be the best-in-class treatment for patients with ROS1- or NTRK-driven tumors, including patients who are TKI-naïve and TKI-pretreated,” said Athena Countouriotis, M.D., president and chief executive officer. “Additionally, we recently received FDA feedback that may provide a faster path to potential approval, including pooling of patients from the Phase 1 portion of the study treated at the recommended dose of repotrectinib with patients treated in the Phase 2 portion, and cohort sample size modifications. Hence, we are modifying the TRIDENT-1 study sample sizes and adding new interim analyses that may support approval into two of our ROS1-positive TKI-pretreated patient cohorts. We now anticipate providing an update in early 2021 on the overall study timelines.”

Early Interim Phase 2 Data from TRIDENT-1 Study
The early Phase 2 TRIDENT-1 dataset utilizing a July 10, 2020 data cutoff includes the first 39 treated patients who have had at least one post-baseline scan. Responses were confirmed with a subsequent scan at least 28 days later per RECIST 1.1 and were determined by physician assessment. Patients were enrolled across six countries.

Phase 2 Preliminary Efficacy Analysis (n=39)

- Across all cohorts reported, median follow-up was 3.6 months (range: 0.4 – 7.4+), and median duration of treatment was 3.7 months (range: 0.7-8.2+)
- In the ROS1-positive TKI-naïve non-small cell lung cancer (NSCLC) population (**EXP-1: n=7**):
    - Six patients achieved a confirmed response for an Objective Response Rate (ORR) of 86 percent. The duration of response ranged from 0.9+ to 2.0+ months and all patients who achieved a response remained in a response at the time of the data cutoff.
        - Since the July 10 data cutoff, the seventh patient in this cohort has achieved an unconfirmed partial response and remains on treatment awaiting a confirmatory scan.
- In the ROS1-positive NSCLC population pretreated with one prior TKI with prior chemotherapy (**EXP-2: n=5**):
    - Two patients achieved a confirmed response for an ORR of 40 percent. The durations of response were 4.5 and 5.6+ months at the time of the data cutoff.

- In the ROS1-positive NSCLC population pretreated with one prior TKI without prior chemotherapy (**EXP-4: n=6**):
    - Four patients achieved a confirmed response for an ORR of 67 percent. The duration of response ranged from 1.0+ to 5.7+ months with all four patients remaining in a response at the time of the data cutoff.
- In the ROS1-positive NSCLC population pretreated with two prior TKIs with prior chemotherapy (**EXP-3: n=10**):
    - No objective responses were observed within this heavily pretreated fourth-line patient population, yet five patients achieved stable disease.
    - The company recently recommended to the study's data monitoring committee (DMC) that expansion cohort three (EXP-3) be modified to remove the requirement for prior chemotherapy based on limited activity to date in this fourth-line patient cohort. The company's intent is to only support third-line patients in this cohort going forward and to preserve the opportunity to evaluate these patients as the treatment landscape changes with less chemotherapy use. The DMC recommended the study proceed and agreed with the recommended change to cohort three.
- In the ROS1-positive NSCLC population pretreated with two prior TKIs without prior chemotherapy (patients enrolled under the initial protocol and analyzed for efficacy in a separate cohort, **EXP-Other: n=5**):
    - Two patients achieved a confirmed response for an ORR of 40 percent. Both patients remained in a response with a duration of 1.9+ months at the time of the data cutoff.
- In the NTRK-positive TKI-pretreated solid tumor population (**EXP-6: n=6**):
    - Three patients achieved a confirmed response for an ORR of 50 percent. The duration of response ranged from 1.7+ to 3.6+ months with all three patients remaining in a response at the time of the data cutoff.

Data from the Phase 1 (at all doses studied) and Phase 2 of the TRIDENT-1 study are summarized in the table below.

TRIDENT-1 Study of Repotrectinib (Phase 2 Cohorts)	**Phase 1** July 22, 2019 Data Cutoff All doses studied, BICR		**Phase 2** July 10, 2020 Data Cutoff Phase 2 Dose, PI assessment	
	ORR	95% CI	ORR	95% CI
ROS1+ TKI-Naïve (EXP-1)	**91% (10/11)**	(59-100)	**86%**[1] **(6/7)**	(42-100)
ROS1+ TKI-Pretreated 1-prior TKI, with prior platinum-based chemotherapy (EXP- 2)	**36% (5/14)**	(13-65)	**40% (2/5)**	(5-85)
ROS1+ TKI-Pretreated, without prior platinum-based chemotherapy (EXP-4)	**50% (2/4)**	(7-93)	**67% (4/6)**	(22-96)
ROS1+ TKI-Pretreated 2-prior TKIs, without prior platinum-based chemotherapy [2] **(EXP- Other)**	**0% (0/1)**	NA	**40% (2/5)**	(5-85)

NTRK TKI-Pretreated (EXP-6)	**33% (1/3)**	(1-91)	**50% (3/6)**	(12-88)

[1] Since the July 10th data cutoff, the seventh patient in this cohort has achieved an unconfirmed partial response and remains on treatment awaiting a confirmatory scan.

[2] Represents the planned modified EXP-3 cohort of patients previously treated with 2 prior TKIs without prior chemotherapy. In EXP-3 (Two prior TKIs with prior chemotherapy; N=10): No objective responses observed.

Data pooled from the Phase 1 (patients dosed at or above the Phase 2 dose) and Phase 2 portions of the TRIDENT-1 study are summarized in the table below.

TRIDENT-1 Study of Repotrectinib (Phase 2 Cohorts)	**Phase 1 + 2 TRIDENT-1 Data Combined** (Phase 1 patients dosed at or above the Phase 2 dose)	
	ORR	95% CI
ROS1+ TKI-Naïve (EXP-1)	**86%[1] (12/14)**	(57-98)
ROS1+ TKI-Pretreated 1-prior TKI, with prior platinum-based chemotherapy (EXP-2)	**50% (6/12)**	(21-79)
ROS1+ TKI-Pretreated 1-prior TKI without prior platinum-based chemotherapy (EXP-4)	**67% (6/9)**	(30-93)
ROS1 TKI-Pretreated 2-prior TKIs, without prior platinum-based chemotherapy [2] (EXP-Other)	**33% (2/6)**	(4-78)
NTRK TKI-Pretreated (EXP-6)	**43% (3/7)**	(10-82)

[1] Since the July 10th data cutoff, one additional Phase 2 patient achieved an unconfirmed partial response and remains on treatment awaiting a confirmatory scan.

[2] Represents the planned modified EXP-3 cohort of patients previously treated with 2 prior TKIs without prior chemotherapy. In EXP-3 (Two prior TKIs with prior chemotherapy; N=10): No objective responses observed.

Preliminary Safety Analysis (n=39)

- A total of 39 *ROS1*- and *NTRK*-positive patients were treated with repotrectinib at a starting dose of 160 mg daily (QD), with 90 percent of patients escalating after 14 days to 160 mg twice daily (BID) per the study defined dose titration approach.

- Repotrectinib was generally well tolerated. The majority of treatment emergent adverse events (TEAEs) were Grade 1 or 2. The TEAEs (any Grade) found in greater than 25 percent of patients were dizziness (62%), fatigue (39%), constipation (33%), dysgeusia (33%), and dyspnea (28%). There were no Grade 3 cases of dizziness and no cases of dizziness leading to treatment discontinuation.

- Additionally, the majority of treatment related adverse events (TRAEs) were Grade 1 or 2. There were no Grade 4 or Grade 5 TRAEs.

Regulatory and Study Updates:
Turning Point also announced recent feedback received from the FDA and modifications the company is making to the study design that may accelerate the timelines to potential approval for repotrectinib. The FDA reiterated that the adequacy of the data to support approval will depend upon the observed ORR and the duration of response assessed in the context of available therapy in a risk-benefit analysis during NDA review.

These updates include:

- Phase 2 cohort sample sizes to support potential approval may include Phase 1 patients treated at the recommended Phase 2 dose. The pooling of Phase 1 and Phase 2 data may shorten timelines to potential regulatory submission based on fewer patients from the Phase 2 portion of the study.

- EXP-2 Cohort (ROS1 TKI-Pretreated with one prior TKI and one platinum-based regimen): The company plans to decrease the sample size from current target of 100 patients to 60 total patients with one formal interim analysis after approximately 30 patients. FDA provided guidance that 6 months of follow up may be sufficient to support approval.

- EXP-4 Cohort (ROS1 TKI-Pretreated with one prior TKI and no prior chemotherapy): The company plans to increase the sample size to a target of 60 patients with one formal interim analysis after approximately 30 patients. Previously, EXP-4 was an exploratory cohort in this patient population. FDA provided guidance that 6 months of follow up may be sufficient to support approval.

- EXP-5 and EXP-6 Cohorts (TRK TKI-Naïve and TKI-Pretreated): FDA provided guidance that 9 months and 6 months of follow up, respectively, from the last response may be sufficient to support approval. Previous guidance was 12 months for both patient cohorts.

Based on this FDA feedback and the subsequent sample size changes, the company is reviewing its timelines for when it expects the top-line interim analysis data sets will be achieved, and anticipates sharing those timelines as it gets closer to achieving full site activation in early 2021.

Webcast and Conference Call
Turning Point will host a webcast accompanied by a slide presentation to discuss the results at 8:00 a.m. EDT/5:00 a.m. PDT. Dr. Countouriotis will host the call, which 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 5077833. 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 and SRC, 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 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 repotrectinib, the results, conduct, progress and timing of the TRIDENT-1 clinical study, plans regarding future regulatory submissions and the regulatory approval path for repotrectinib. 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.

Contact:
Jim Mazzola
jim.mazzola@tptherapeutics.com
858-342-8272