Instructions: Submit completed form after screening assessments are complete and subject meets all respective eligibility criteria. Submit to TRIDENT.eligibility@premier-research.com, TRIDENT.eligibility@tptherapeutics.com, and your CRA at least 2 business days prior to planned Cycle 1 Day 1. Investigator (PI or Sub-I) signature required. Enrollment cannot occur until approval is granted by Premier and/or Turning Point Medical via endpoint IRT.

Site Number (####)	___ ___ ___ ___	**Subject ID** (####-####)	___ ___ ___ ___ - ___ ___ ___ ___
PI Last Name		**Year of Birth** (yyyy) & **Age**	___ ___ ___ ___ Year of Birth / ___ ___ Age
Country	FRANCE	**Main Consent Date** (dd-MON-yyyy)	___ ___ - ___ ___ ___ - ___ ___ ___ ___
Sex	☐ Male Female ☐	**IRB/EC Approved Protocol Version**	7.0 France 27FEB2020
Check only if Re-screen	☐ Yes	**Planned C1D1 Date** (dd-MON-yyyy)	___ ___ - ___ ___ ___ - ___ ___ ___ ___

Select Expansion Cohort for Enrollment of Subject:

Category	ROS1+ Advanced NSCLC			NTRK+ Advanced Solid Tumors	
Cohort	**EXP-1**	**EXP-2**	**EXP-3**	**EXP-5**	**EXP-6**
Prior TKI Treatment	Treatment Naïve	1 Prior	2 Prior	Treatment Naïve	1 or 2 Prior *Pre-Treated*
Prior Chemo and/or Immunotherapy	≤ 1 prior	=1 prior Platinum based	=1 prior Platinum based	Any Number	Any Number
Cancer Type	ROS1+ advanced NSCLC	ROS1+ advanced NSCLC	ROS1+ advanced NSCLC	NTRK+ Advanced Solid Tumors	NTRK+ Advanced Solid Tumors
Cohort for Enrollment	☐	☐	☐	☐	☐

Include the following de-identified information as attachments to the Enrollment Eligibility Form:

Documentation (Screening)*	**Form/Vendor**	**Report Included**
1. Local Molecular Report *(ROS1, NTRK fusion)*	Local	☐
2. Confirmation of Tumor Molecular Alteration ***(Central Read)***	Almac Central Read	☐
3. Imaging Report – *Local* ***(Local)***	Local	☐
4. Imaging Report – *Central* ***(PAREXEL – BICR/Central Read)***	PAREXEL Central Read	☐
5. Laboratory Reports *(Include results of troponin or confirmation of collection)*	ICON Central Lab	☐
6. ECG Tracing (triplicate) *(from ERT machine printout)*		☐
7. Prior Therapy Form – List all prior cancer therapies and surgeries *(Turning Point also submits to PAREXEL with Screening Imaging)*	***Prior Therapy Form***	☐
8. Concomitant Medications List with start/stop dates		☐
9. Medical History		☐

*Key eligibility information on source documents should be translated to English by site staff, as applicable

Cancer Details			
Primary cancer diagnosis			
Gene fusion			
Local Lab Name			
Local Testing Method	☐ NGS	☐qPCR	☐FISH

Site Number (####)	___ ___ ___ ___	**Subject ID** (####-####)	___ ___ ___ ___ - ___ ___ ___ ___

Inclusion Criteria	**Yes**	**No**
1. Histologically or cytologically confirmed diagnosis of locally advanced, or metastatic solid tumor (including primary CNS tumors) that harbors a *ROS1, ALK or NTRK1-3* gene fusion.	☐	☐
2. Subject must have a documented *ROS1, ALK or NTRK1-3* gene fusion that has been identified by *local testing* AND that has been **prospectively confirmed** by a *central diagnostic laboratory* selected by the Sponsor to determine molecular eligibility **PRIOR to enrollment.** • *Local testing* is defined as a test performed in a Clinical Laboratory Improvement Amendments (CLIA) laboratory or equivalently accredited diagnostic laboratory. The following test modalities are permitted: o Tissue-based or liquid biopsy next-generation sequencing (NGS) or quantitative polymerase chain reaction (qPCR) o Fluorescence in situ hybridization (FISH) • The *central diagnostic laboratory test* selected by the Sponsor will be used to determine molecular eligibility for enrollment: o Adequate tumor tissue needs to be sent to the Sponsor designated central diagnostic laboratory for *ALK, ROS1, or NTRK* gene fusion status confirmation PRIOR to enrollment. In cases where archived tumor tissue is not available, a de novo biopsy should be obtained for this purpose. **See the Study Laboratory Manual for details.**	☐	☐
3. Eastern Cooperative Oncology Group (ECOG) Performance Status 0–1	☐	☐
ECOG Score:	_____	
4. Age ≥18 (or age ≥ 20 as required by local regulation).	☐	☐
5. Willing and able to provide written institutional review board (IRB)/institutional ethics committee-approved Informed Consent	☐	☐
6. At least 1 measurable target lesion according to RECIST (v1.1) **prospectively** confirmed by Blinded Independent Central Radiology Review (BICR), selected by the Sponsor, PRIOR to enrollment. Subjects with CNS-only measurable target lesion ≥10 mm as defined by RECIST (v1.1) are eligible.	☐	☐

Site Number (####)	___ ___ ___ ___	**Subject ID** (####-####)	___ ___ ___ ___ - ___ ___ ___ ___

Inclusion Criteria	**Yes**	**No**
7. Subjects with advanced solid tumors harboring ALK, ROS1, NTRK1, NTRK2, or NTRK3 rearrangement will be assigned into 6 distinct expansion (EXP) cohorts provided all inclusion and exclusion criteria are met:	☐	☐
	SELECT BELOW	
• **EXP-1: ROS1 TKI-naïve *ROS1+* NSCLC (n=55).** o No prior exposure to a ROS1 TKI is allowed. o Up to one prior line of chemotherapy OR immunotherapy is allowed (chemo- or immunotherapy-based combination regimen is considered as one line of treatment).	EXP-1 ☐	
• **EXP-2: 1 Prior ROS1 TKI AND 1 Platinum Based Chemotherapy/Immunotherapy *ROS1+* NSCLC (n=100).** o Disease progression, unresponsive, or intolerant to one prior line of a ROS1 TKI. o ROS1 TKIs used in a prior line of treatment are limited to crizotinib, ceritinib, entrectinib, or lorlatinib. Note: Any previous exposure to a ROS1 TKI is considered as one prior line of TKI treatment (e.g., if the same ROS1 TKI was given before and after a chemotherapy or other systemic therapy, it is considered as 2 prior TKIs and the subject would not be eligible for EXP-2). o In addition, the subject must have received one prior line of platinum-based chemotherapy OR one prior line of platinum-based chemotherapy in combination with immunotherapy before or after a ROS1 TKI (Note: subject is not eligible if he/she has been treated with more than one line of chemotherapy OR has received immunotherapy alone).	EXP-2 ☐	
• **EXP-3: 2 Prior ROS1 TKIs AND 1 Platinum Based Chemotherapy/Immunotherapy ROS1+ NSCLC (n=40).** o Disease progression, unresponsive, or intolerant to 2 prior lines of a ROS1 TKI treatment. o ROS1 TKIs used in prior lines of treatment are limited to crizotinib, ceritinib, entrectinib, lorlatinib, brigatinib, ensartinib, or cabozantinib. Other prior ROS1 TKI agents that are not listed may be allowed after discussion with the Sponsor Medical Monitor. Note: Any previous exposure to a ROS1 TKI is considered as one prior line of TKI treatment (e.g., if 2 different ROS1 TKIs are utilized, or the same ROS1 TKI was given before and after a chemotherapy or other systemic therapy, it is considered as 2 prior TKIs and the subject would be eligible). o In addition, the subject must have received one prior line of platinum-based chemotherapy OR one prior line of platinum-based chemotherapy in combination with immunotherapy before or after a ROS1 TKI (Note: subject is not eligible if he/she has been treated with more than one line of chemotherapy OR has received immunotherapy alone). o	EXP-3 ☐	
~~• **EXP-4: ROS1 or ALK TKI-naïve *ROS1+* or *ALK+* solid tumors (non-NSCLC) (n=12-26).**~~ ~~o No prior exposure to a ROS1 or ALK TKI is allowed.~~ ~~o Up to 2 prior lines of chemo or immunotherapy are allowed (chemo- or immunotherapy-based combination regimen is considered as one line of treatment).~~	~~EXP-4~~ ~~☐~~	

Site Number (####)	___ ___ ___ ___	**Subject ID** (####-####)	___ ___ ___ ___ - ___ ___ ___ ___

Inclusion Criteria	**Yes**	**No**
• **EXP-5**: **TRK TKI-naïve *NTRK+* solid tumors (n=55)**. o No prior exposure to a TRK TKI is allowed. o Prior lines on chemotherapy or immunotherapy are allowed. Disease progression on prior systemic therapy is required unless no appropriate therapeutic alternative exists.	EXP-5 ☐	
• **EXP-6**: **TRK TKI-pretreated *NTRK+* solid tumors (n=40).** o Disease progression, unresponsive, or intolerant to 1 or 2 prior TRK TKIs. o TRK TKIs used in prior lines of treatment are limited to entrectinib, larotrectinib, or LOXO-195. Other prior TRK TKIs that are not listed may be allowed after discussion with the Sponsor Medical Monitor. Note: Any previous exposure of a TRK TKI is considered as one prior line of TKI treatment, (e.g., if 2 different TRK TKIs are utilized or the same TRK TKI was used before and after a chemo- or other systemic therapy, it is counted as 2 prior TKIs and the subject would be eligible). o Any prior lines of chemo- or immunotherapy are allowed.	EXP-6 ☐	
8. Required wash-out time that is related to prior therapies before starting repotrectinib treatment: • If the immediate prior treatment was a ROS1 or TRK TKI: Approximately 5 half-lives must have elapsed since completion of treatment with the last TKI for subjects enrolling into the pretreated expansion cohorts (EXP-2, -3, and -6). All side effects from prior treatments with a ROS1 or TRK TKI must have resolved to grade ≤ 1 prior to starting treatment with repotrectinib. • Approximately 5 half-lives must have elapsed after discontinuation of prior systemic chemotherapy (or at least 42 days for prior nitrosoureas and mitomycin C) and all side effects from prior treatments must have resolved to grade ≤1 with the exception of alopecia. • Approximately 5 half-lives must have elapsed after discontinuation of prior immunotherapy and all immune-related side effects from prior immunotherapy must have resolved to grade ≤1.	☐	☐
9. Subjects with asymptomatic CNS metastases (treated or untreated) and/or asymptomatic leptomeningeal carcinomatosis are eligible to enroll if they satisfy the following criteria: • Subjects requiring steroids at a stable or decreasing dose (≤ 12 mg/day dexamethasone or equivalent) for at least 14 days. • Subjects on stable doses of levetiracetam (same dose for 14 days). • A minimum of 14 days must have elapsed from the completion of whole brain radiation treatment (WBRT) before the start of treatment with repotrectinib, and all side effects (with the exception of alopecia) from WBRT are resolved to grade ≤1. • A minimum of 7 days must have elapsed from the completion of stereotactic radiosurgery before the start of treatment with repotrectinib, and all side effects (with the exception of alopecia) from stereotactic radiosurgery are resolved to grade ≤1.	☐	☐
10. Baseline laboratory values fulfilling the following requirements	☐	☐

Absolute Neutrophils Count (ANC)	≥1,500/mm^3 (1.5 x 10^9/L)
Platelets (PLT)	≥100,000/mm^3 (100 x 10^9/L) independent of platelets transfusion support for at least 7 days prior to dosing

Site Number (####)	___ ___ ___ ___	**Subject ID** (####-####)	___ ___ ___ ___ - ___ ___ ___ ___

Inclusion Criteria		**Yes**	**No**
Hemoglobin	≥ 9.0 g/dL independent of transfusion support for at least 7 days prior to dosing		
Creatinine Clearance*	Within Normal Limits > 40 mL/min		
Total Serum Bilirubin	<1.5 x ULN		
Liver Transaminases (AST/ALT)	<2.5 x ULN; < 5 x ULN if liver metastases are present		
Alkaline Phosphatase (ALP)	<2.5 x ULN; < 5 x ULN if liver and/or bone metastasis are present.		
Serum calcium, magnesium and potassium	Normal or CTCAE grade ≤ 1 with or without supplementation.		
AST/ALT = aspartate aminotransferase/alanine aminotransferase, ULN = upper limit of normal * calculated by Cockcroft and Gault's formula: (140 - age [yr]) x body weight [Kg] x 1.23 x (0.85 if female) /serum creatinine [µmol/L].			
11. **<u>Women of childbearing potential (WOCBP)</u>** must have a negative serum pregnancy test during screening and be neither breastfeeding nor intending to become pregnant during study participation. Female patients will be considered to be of childbearing potential unless they have undergone permanent contraception or are postmenopausal. Postmenopausal is defined as at least 12 months without menses with no other medical reasons (e.g., chemical menopause due to anticancer treatment). For WOCBP and for male subjects with pregnant or nonpregnant WOCBP partners, agreement must be made to use highly effective contraceptive methods from the time of screening throughout the study until 3 months (WOCBP) or 6 months (men) after administration of the last dose of any study medication. Highly effective contraceptive methods consist of prior sterilization, intra-uterine device (IUD), intrauterine hormone-releasing system (IUS), oral or injectable contraceptives, and/or barrier methods. Abstinence alone might not be considered an adequate contraceptive measure for the purposes as per local regulations.		☐	☐
12. Ability to swallow capsules intact (without chewing, crushing, or opening).		☐	☐
13. Life expectancy ≥ 3 months.		☐	☐
14. Willingness and ability to comply with scheduled visits, treatment plan, laboratory tests, and other study procedures.		☐	☐

Exclusion Criteria	**Yes**	**No**
1. Concurrent participation in another therapeutic clinical trial.	☐	☐
2. Symptomatic brain metastases or leptomeningeal involvement.	☐	☐
3. History of previous cancer requiring therapy within the previous 2 years, except for squamous cell or basal-cell carcinoma of the skin, or any in situ carcinoma that has been completely resected.	☐	☐
4. Major surgery within 4 weeks of start of repotrectinib treatment. Radiation therapy (except palliative to relieve bone pain) within 2 weeks of study entry. Palliative radiation (≤10 fractions) must have been completed at least 48 hours prior to study entry.	☐	☐
5. Clinically significant cardiovascular disease (either active or within 6 months prior to enrollment): myocardial infarction, unstable angina, coronary/peripheral artery bypass graft, symptomatic congestive heart failure (New York Heart Association Classification Class ≥ II), cerebrovascular accident or transient ischemic attack, symptomatic bradycardia,	☐	☐

Site Number (####)	___ ___ ___ ___	**Subject ID** (####-####)	___ ___ ___ ___ - ___ ___ ___ ___

Exclusion Criteria	**Yes**	**No**
requirement for anti-arrhythmic medication. Ongoing cardiac dysrhythmias of CTCAE grade ≥2.		
6. Any of the following cardiac criteria: • Mean resting corrected QT interval (ECG interval measured from the onset of the QRS complex to the end of the T wave) for heart rate (QTc) > 470 msec obtained from 3 ECGs, using the screening clinic ECG machine-derived QTc value • Any clinically important abnormalities in rhythm, conduction or morphology of resting ECG (e.g., complete left bundle branch block, third degree heart block, second degree heart block, PR interval > 250 msec) • Any factors that increase the risk of QTc prolongation or risk of arrhythmic events such as heart failure, hypokalemia, congenital long QT syndrome, family history of long QT syndrome, or any concomitant medication known to prolong the QT interval	☐	☐
7. Known active infections requiring ongoing treatment (bacterial, fungal, viral including HIV positivity).	☐	☐
8. Gastrointestinal disease (e.g., Crohn's disease, ulcerative colitis, or short gut syndrome) or other malabsorption syndromes that would impact on drug absorption.	☐	☐
9. Peripheral neuropathy, paresthesia, dizziness, dysgeusia, muscle weakness, ataxia grade ≥2.	☐	☐
10. History of extensive, disseminated, bilateral, or presence of CTCAE grade 3 or 4 interstitial fibrosis or interstitial lung disease including a history of pneumonitis, hypersensitivity pneumonitis, interstitial pneumonia, interstitial lung disease, obliterative bronchiolitis, and pulmonary fibrosis. Subjects with history of prior radiation pneumonitis are not excluded.	☐	☐
11. Other severe acute or chronic medical or psychiatric condition or laboratory abnormality that may increase the risk associated with study participation or study drug administration, or that may interfere with the interpretation of study results and, in the judgment of the Investigator, would make the subject inappropriate for entry into this study, or could compromise protocol objectives in the opinion of the Investigator and/or Turning Point Therapeutics.	☐	☐
12. Current use or anticipated need for drugs that are known to be strong CYP3A inhibitors or inducers as listed in **Error! Reference source not found.**.	☐	☐

Did Patient Satisfy ALL Inclusion/Exclusion Criteria? *(per current approved protocol version)* *If no, explain below and identify criteria*	☐ Yes	☐ No

		___ ___ - ___ ___ ___ - ___ ___ ___ ___
Investigator/Sub-Investigator Name	**Investigator/Sub-Investigator Signature**	**Date** (dd-MON-yyyy)

Site Number (####)	___ ___ ___ ___	**Subject ID** (#####-####)	___ ___ ___ ___ - ___ ___ ___ ___

Turning Point Therapeutics (Or Designee) ONLY Below This Line

PATIENT APPROVED FOR ENROLLMENT *Include any relevant comments below, if applicable*

		___ ___ - ___ ___ ___ - ___ ___ ___ ___
Approver Name	**Signature**	**Date** (dd-MON-yyyy)