ForPatients
by Roche

NeoplasmsRespiratory Tract NeoplasmsGastrointestinal CancerNon-Small Cell Lung Cancer (NSCLC)Lung NeoplasmNon Small Cell Lung CarcinomaNeuroendocrine CarcinomaSolid TumorsCarcinomaAdenocarcinomaMedullary Thyroid CancerThoracic NeoplasmsTumorThyroid CancerHead and Neck Neoplasms

Phase 1/2 Study of the Highly-selective RET Inhibitor, Pralsetinib (BLU-667), in Patients With Thyroid Cancer, Non-Small Cell Lung Cancer, and Other Advanced Solid Tumors

Phase 1/2 Study of the Highly-selective RET Inhibitor, Pralsetinib (BLU-667), in Participants With Thyroid Cancer, Non-Small Cell Lung Cancer, and Other Advanced Solid Tumors

Trial Status	Trial Runs In	Trial Identifier
Completed	13 Countries	NCT03037385 2016-004390-41 BLU-667-1101 BO42863

The information is taken directly from public registry websites such as ClinicalTrials.gov, EuClinicalTrials.eu, ISRCTN.com, etc., and has not been edited.

Official Title:

A Phase 1/2 Study of the Highly-selective RET Inhibitor, BLU-667, in Patients With Thyroid Cancer, Non-Small Cell Lung Cancer (NSCLC) and Other Advanced Solid Tumors

Trial Summary:

This is a Phase 1/2, open-label, first-in-human (FIH) study designed to evaluate the safety, tolerability, pharmacokinetics (PK), pharmacodynamics (PD), and preliminary antineoplastic activity of pralsetinib (BLU-667) administered orally in participants with medullary thyroid cancer (MTC), RET-altered NSCLC and other RET-altered solid tumors.

Hoffmann-La Roche Sponsor	**Phase 1/Phase 2** Phase

NCT03037385 2016-004390-41 BLU-667-1101 BO42863
Trial Identifiers

Eligibility Criteria:

Gender	Age	Healthy Volunteers
All	#18 Years	No

Inclusion Criteria:

- Diagnosis during dose escalation (Phase 1) - Pathologically documented, definitively diagnosed non-resectable advanced solid tumor.
- All participants treated at doses > 120 mg per day must have MTC, or a RET-altered solid tumor per local assessment of tumor tissue and/or blood.
- Diagnosis during dose expansion (Phase 2) - All participants (with the exception of participants with MTC enrolled in Groups 3, 4, and 9) must have an oncogenic RET-rearrangement/fusion or mutation (excluding synonymous, frameshift, and nonsense mutations) solid tumor, as determined by local or central testing of tumor or circulating tumor nucleic acid in blood; as detailed below.
- Group 1 - participants must have pathologically documented, definitively diagnosed locally advanced or metastatic NSCLC with a RET fusion previously treated with a platinum-based chemotherapy.
- Group 2 - participants must have pathologically documented, definitively diagnosed locally advanced or metastatic NSCLC with a RET fusion not previously treated with a platinum-based chemotherapy, including those who have not had any systemic therapy. Prior platinum chemotherapy in the neoadjuvant and adjuvant setting is permitted if the last dose of platinum was 4 months or more before the first dose of study drug.
- Group 3 - participants must have pathologically documented, definitively diagnosed advanced MTC that had progressed within 14 months prior to the Screening Visit and was previously treated with cabozantinib and/or vandetanib.
- Group 4 - participants must have pathologically documented, definitively diagnosed advanced MTC that had progressed within 14 months prior to the Screening Visit and was not previously treated with cabozantinib and/or vandetanib.
- Group 5 - participants must have a pathologically documented, definitively diagnosed advanced solid tumor with an oncogenic RET fusion, have previously received standard of care (SOC) appropriate for their tumor type (unless there is no accepted standard therapy for the tumor type or the Investigator has determined that treatment with standard therapy is not appropriate), and must not have been eligible for any of the other groups.
- Group 6 - participants must have a pathologically documented, definitively diagnosed advanced solid tumor with an oncogenic RET fusion or mutation that was previously treated with a selective tyrosine kinase inhibitor (TKI) that inhibits RET
- Group 7 - participants must have a pathologically documented, definitively diagnosed advanced solid tumor with an oncogenic RET mutation previously treated with SOC appropriate for the tumor type and not eligible for any of the other groups
- Group 8 - participants must have pathologically documented, definitively diagnosed locally advanced or metastatic NSCLC with a RET fusion that was previously treated with a platinum based chemotherapy (China only).
- Group 9 - participants must have pathologically documented, definitively diagnosed advanced MTC that had progressed within 14 months prior to the Screening Visit, and was not previously treated with systemic therapy (except prior cytotoxic chemotherapy is allowed) for advanced or metastatic disease (China only).
- Participants must have non-resectable disease.
- Dose expansion (Phase 2): Participants in all groups (except Group 7) must have measurable disease per RECIST v1.1 (or RANO, criteria if appropriate for tumor type).
- Participants agrees to provide tumor tissue (archived, if available or a fresh biopsy) for RET status confirmation and is willing to consider an on-treatment tumor biopsy, if considered safe and medically feasible by the treating Investigator. For Phase 2, Group 6, participants are required to undergo a pretreatment biopsy to define baseline RET status in tumor tissue.
- Participants has Eastern Cooperative Oncology Group (ECOG) performance status (PS) of 0-1.

Exclusion Criteria:

- Participant's cancer has a known primary driver alteration other than RET. For example, NSCLC with a targetable mutation in EGFR, ALK, ROS1 or BRAF; colorectal with an oncogenic KRAS, NRAS, or BRAF mutation.
- Participants had any of the following within 14 days prior to the first dose of study drug:
- Platelet count < 75 × 10^9/L.
- Absolute neutrophil count < 1.0 × 10^9/L.
- Hemoglobin < 9.0 g/dL (red blood cell transfusion and erythropoietin may be used to reach at least 9.0 g/dL, but must have been administered at least 2 weeks prior to the first dose of study drug.
- Aspartate aminotransferase (AST) or alanine aminotransferase (ALT) > 3 × the upper limit of normal (ULN) if no hepatic metastases are present; > 5 × ULN if hepatic metastases are present.
- Total bilirubin > 1.5 × ULN; > 3 × ULN with direct bilirubin > 1.5 × ULN in presence of Gilbert's disease.
- Estimated (Cockcroft-Gault formula) or measured creatinine clearance < 40 mL/min.
- Total serum phosphorus > 5.5 mg/dL
- QT interval corrected using Fridericia's formula (QTcF) > 470 msec or history of prolonged QT syndrome or Torsades de pointes, or familial history of prolonged QT syndrome.
- Clinically significant, uncontrolled, cardiovascular disease.
- Central nervous system (CNS) metastases or a primary CNS tumor that is associated with progressive neurological symptoms.
- Clinically symptomatic interstitial lung disease or interstitial pneumonitis including radiation pneumonitis
- Participants in Groups 1-5 and 7 (Phase 2) previously treated with a selective RET inhibitor
- Participant had a major surgical procedure within 14 days of the first dose of study drug
- Participant had a history of another primary malignancy that had been diagnosed or required therapy within the a year prior to the study
- Pregnant or breastfeeding female participants