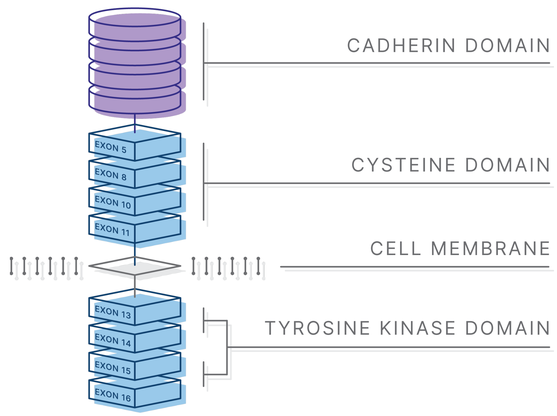
# A targeted therapy for *RET* fusion positive NSCLC is here

## Making a difference for patients with NSCLC

## What Is *RET*?

The *RET* (Rearranged during Transfection) gene encodes a transmembrane receptor tyrosine kinase.[1] RET acts as a receptor for Glial cell line-derived neurotrophic Family Ligands (GFL), a group of soluble neurotrophic factors that are highly important during embryogenesis and human development.[2,3]

### RET: Three Isoforms With a Cytoplasmic Kinase Domain

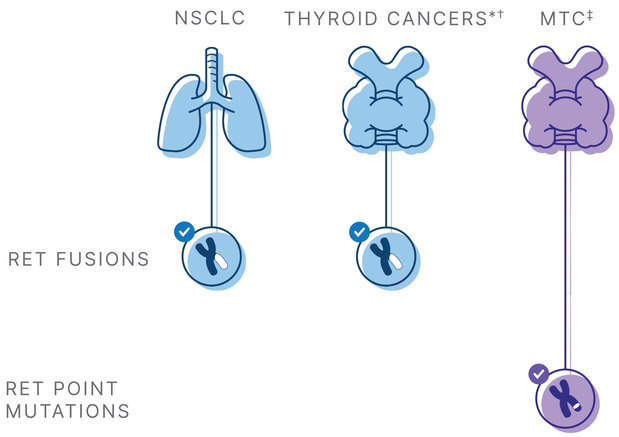



## *RET* in Oncogenesis

Oncogenic activation of *RET* by in-frame gene fusions or activating point mutations are implicated in the pathogenesis of multiple cancers.[4-7]

In NSCLC, *RET* is a primary oncogenic driver with *RET* fusions occurring in up 2% of cases.[4,14] *RET* is known to partner with at least 12 different genes, with *KIF5B-RET* being the most frequently observed *RET* fusion in NSCLC.[15,16]

### *RET*-Driven Cancers




*Other than MTC: includes papillary, poorly differentiated, anaplastic, and Hurthle cell thyroid cancers

†*RET* fusions also occur in 10-20% of papillary thyroid cancers (PTC)[4,8,9]

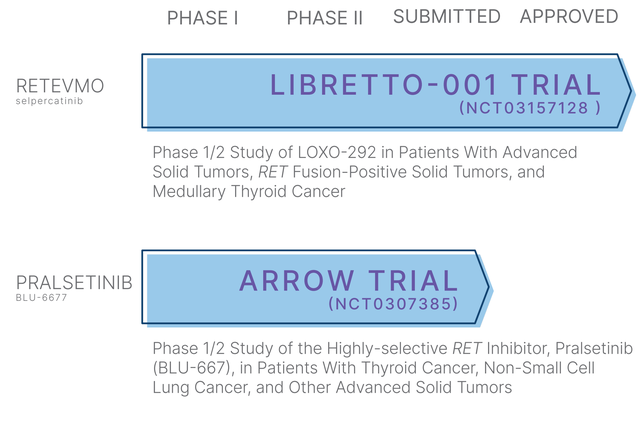
‡Medullary thyroid cancer: *RET* point mutations affect most MTCs [4,6,9]

## New Selective *RET* Inhibitor Therapies

Novel highly selective *RET* targeted agents have been tested in *RET* driven NSCLC, advancing targeted treatments over MKIs such as cabozantinib and vandetanib.[10]

Retevmo™ (selpercatinib) and pralsetinib (BLU-667) are the first targeted agents designed to selectively inhibit *RET*.[11,12]

### Development of Novel Highly Selective *RET* Targeted Agents




Phase 1/2 Study of LOXO-292 in Patients With Advanced Solid Tumors, *RET* Fusion-Positive Solid Tumors, and Medullary Thyroid Cancer

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

In the LIBRETTO-001 study for Retevmo, *RET* fusions were detected in 90% of patients using NGS compared to 8.6% using fluorescence in situ hybridization (FISH) and 1.9% using chain reaction (PCR).[13]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