

# Broad Clinical Development Program for Cabozantinib

As of June 6, 2018; for a full list of ongoing studies, please visit [www.clinicaltrials.gov](http://www.clinicaltrials.gov)

SINGLE-AGENT CABOZANTINIB	
Indication	Status Update
<b>Thyroid Cancer</b>	
Progressive, metastatic medullary thyroid cancer	Approved in U.S. and EU (EXAM)
Progressive, metastatic medullary thyroid cancer	Post-marketing study (EXAMINER)
Differentiated thyroid cancer	Phase 2*
<b>Renal Cell Carcinoma (RCC)</b>	
Second- and later-line advanced RCC	Approved in U.S. and EU (METEOR)
Advanced RCC (including previously untreated RCC)	Approved in U.S. on December 19, 2017; Ipsen's filing approved in EU in May 2018 following positive CHMP recommendation
First- or second-line papillary RCC	Randomized phase 2† (PAPMET)
<b>Hepatocellular Carcinoma (HCC)</b>	
Second- and later-line advanced HCC	Phase 3 pivotal trial (CELESTIAL) positive results; sNDA filing accepted in May 2018 with PDUFA date of January 14, 2019; EMA filing accepted for review in March 2018 (Ipsen)
<b>Non-Small Cell Lung Cancer (NSCLC)</b>	
EGFR wild-type	Phase 2†
Molecular alterations in RET, ROS1, MET, AXL, or NTRK1	Phase 2*
<b>Additional Trials</b>	
Metastatic urothelial cancer	Phase 2*
Breast cancer with brain metastases	Phase 2*
Colorectal cancer	Phase 1*
High-grade uterine sarcomas	Phase 2§
Metastatic gastrointestinal stromal tumor	Phase 2 (CABOGIST)§
Pancreatic neuroendocrine tumors and carcinoid tumors	Phase 2†
Plexiform neurofibromas (pediatric and adult cohorts)	Phase 2*
Relapsed osteosarcoma or Ewing sarcoma	Phase 2†
Soft-tissue sarcomas	Phase 2†



\* Trial conducted through our IST program. † Trial conducted through collaboration with NCI-CTEP. § Trial sponsored by the European Organization for Research and Treatment of Cancer.

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### CABOZANTINIB IN COMBINATION WITH IMMUNE CHECKPOINT INHIBITORS

Indication	Combination Regimen	Status Update
<b>RCC</b>		
First-line advanced RCC	+ nivolumab	Phase 3 pivotal trial (CheckMate 9ER)
<b>HCC</b>		
First-line and previously-treated advanced HCC	+ nivolumab ± ipilimumab	Phase 1/2 (Checkmate 040)
Neoadjuvant locally advanced HCC	± nivolumab	Phase 1b*
<b>NSCLC</b>		
Advanced solid tumors	+ atezolizumab	Phase 1b started in 2017, now with eighteen expansion cohorts including NSCLC (COSMIC 021)
<b>Trials in Genitourinary Tumors, including RCC, Urothelial Carcinoma (UC), and Castration-Resistant Prostate Cancer (CRPC)</b>		
Genitourinary tumors	+ nivolumab ± ipilimumab	Phase 1†
Advanced solid tumors	+ atezolizumab	Phase 1b started in 2017, now with eighteen expansion cohorts including RCC, UC, and CRPC (COSMIC 021)
<b>Additional Clinical Trials</b>		
Endometrial cancer	+ nivolumab	Phase 2†
Metastatic, triple negative breast cancer	+ nivolumab	Phase 2*



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