

# GAVRETO™

pralsetinib | 100mg capsules



**GAVRETO™—the only once-daily targeted RET therapy for patients with RET fusion+ metastatic NSCLC.<sup>1</sup>**

## **NATIONAL COMPREHENSIVE CANCER NETWORK® (NCCN®)-RECOMMENDED TREATMENT OPTION**

**NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) recommend pralsetinib (GAVRETO) as a preferred first-line treatment option for RET fusion-positive metastatic NSCLC (NCCN Category 2A)<sup>\*2</sup>**



NCCN=National Comprehensive Cancer Network®; NSCLC=non-small cell lung cancer; RET=rearranged during transfection.

### **INDICATION**

GAVRETO™ (pralsetinib) is indicated for the treatment of adult patients with metastatic rearranged during transfection (RET) fusion-positive non-small cell lung cancer (NSCLC) as detected by an FDA approved test.

This indication is approved under accelerated approval based on overall response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

### **SELECT SAFETY INFORMATION**

**Interstitial Lung Disease (ILD)/ Pneumonitis** occurred in 10% of patients who received GAVRETO, including 2.7% with Grade 3/4, and 0.5% with fatal reactions. Monitor for pulmonary symptoms indicative of ILD/pneumonitis. Withhold GAVRETO and promptly investigate for ILD in any patient who presents with acute or worsening of respiratory symptoms (e.g., dyspnea, cough, and fever). Withhold, reduce dose or permanently discontinue GAVRETO based on severity of confirmed ILD.

**Please see additional Select Safety Information throughout, and click here to see the full [Prescribing Information](#) for GAVRETO.**

\*See the NCCN Guidelines® for NSCLC for detailed recommendations, including other preferred treatment options.

NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.



# GAVRETO was studied in both treatment-naïve and previously platinum-treated NSCLC patients<sup>1</sup>

In preclinical studies, pralsetinib was designed for potent and selective inhibition of RET

## ARROW study design in the NSCLC population

Efficacy and safety with GAVRETO (400 mg orally once daily) was evaluated in patients with RET fusion+ mNSCLC in the ARROW study, a phase 1/2, nonrandomized, open-label, single-arm, multicohort, multicenter clinical trial. Patients with asymptomatic central nervous system metastases, including patients with stable or decreasing steroid use within 2 weeks prior to study entry, were enrolled.

## Demographic characteristics in the NSCLC population at baseline<sup>1,3</sup>

	Treatment-naïve patients (n=27)	Previously platinum-treated patients (n=87)
<b>Median age</b>	65 years (30-87)	60 years (28-85)
<b>Gender</b>	52% female 48% male	49% female 51% male
<b>Race/ethnicity</b>	59% White, 33% Asian, 4% Hispanic/Latino	53% White, 35% Asian, 6% Hispanic/Latino
<b>ECOG status</b>	0-1: 96% 2: 4%	0-1: 94% 2: 6%
<b>RET fusion partner</b>	70% KIF5B 11% CCDC6	75% KIF5B 17% CCDC6
<b>History of or current CNS metastases at baseline</b>	37%	43%
<b>Prior therapy</b>	Per protocol, patients were not eligible for platinum-based chemotherapy based on investigator assessment <sup>3</sup>	45% PD-1/PD-L1 inhibitor, 25% prior kinase inhibitors
<b>Patient identification</b>	67% NGS <ul style="list-style-type: none"> <li>• 41% tumor samples</li> <li>• 22% blood or plasma</li> <li>• 4% unknown</li> </ul> 33% FISH	77% NGS <ul style="list-style-type: none"> <li>• 45% tumor samples</li> <li>• 26% blood or plasma</li> <li>• 6% unknown</li> </ul> 21% FISH 2% other

ECOG=Eastern Cooperative Oncology Group; FISH=fluorescence in situ hybridization; mNSCLC=metastatic non-small cell lung cancer; NGS=next generation sequencing; PD-1/PD-L1=programmed cell death 1/programmed death ligand 1.

## SELECT SAFETY INFORMATION

**Hypertension** occurred in 29% of patients, including Grade 3 hypertension in 14% of patients. Overall, 7% had their dose interrupted and 3.2% had their dose reduced for hypertension. Treatment-emergent hypertension was most commonly managed with anti-hypertension medications. Do not initiate GAVRETO in patients with uncontrolled hypertension. Optimize blood pressure prior to initiating GAVRETO. Monitor blood pressure after 1 week, at least monthly thereafter and as clinically indicated. Initiate or adjust anti-hypertensive therapy as appropriate. Withhold, reduce dose, or permanently discontinue GAVRETO based on the severity.

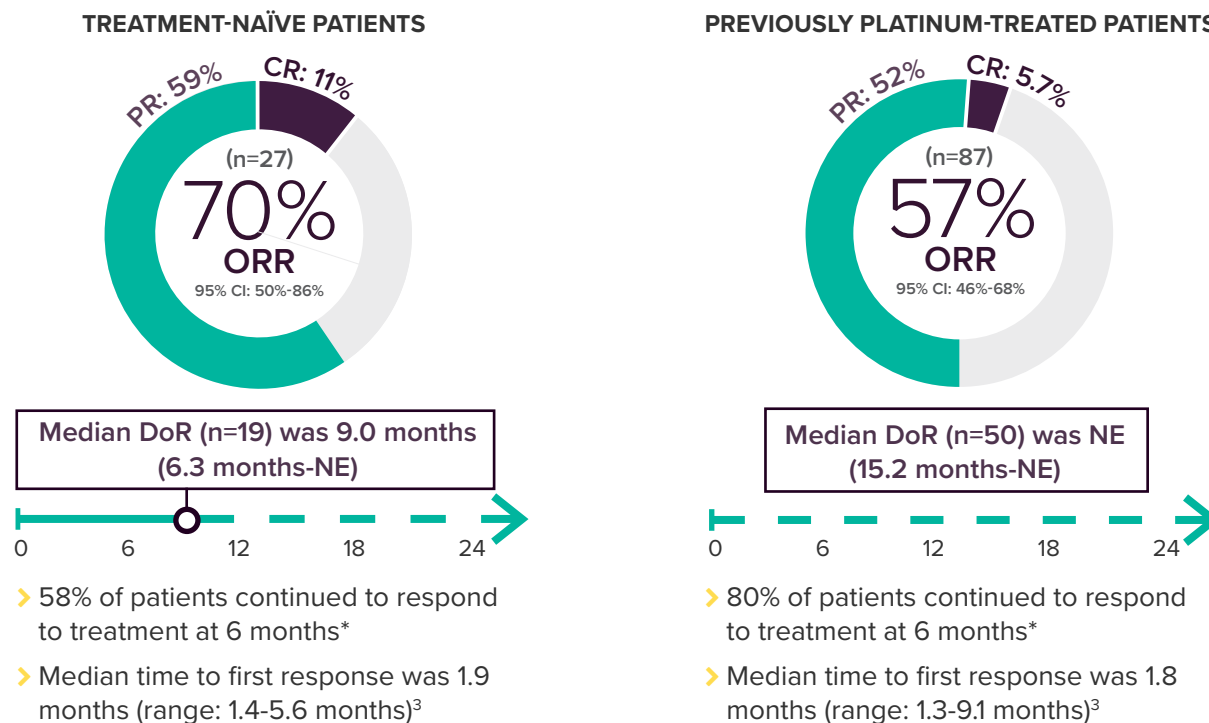
Please see additional Select Safety Information throughout, and click here to see the full [Prescribing Information](#) for GAVRETO.

# GAVRETO demonstrated robust and durable response with or without prior therapy<sup>1</sup>



## Efficacy results with GAVRETO<sup>1,3</sup>

The major efficacy outcome measures were overall response rate (ORR) and duration of response (DoR), as assessed by a blinded independent central review (BICR) according to RECIST v1.1.



## GAVRETO demonstrated consistent response across previously platinum-treated subgroups<sup>1</sup>

**CNS ACTIVITY**

Brain metastases at baseline (n=8)<sup>†</sup>: DoR at 6 months: 75%

**50%** of patients with measurable disease had a response  
2 had CR

**PRIOR PD-1/PD-L1 INHIBITOR** | Exploratory analysis

(n=39): **59% ORR** (95% CI: 42%-74%)

Median DoR was not reached (95% CI: 11.3-NE)

\*Calculated using the proportion of responders with an observed duration of response at least 6 months or greater.

<sup>†</sup>No patients received radiation therapy (RT) to the brain within 2 months prior to study entry.

BICR=blinded independent central review; CI=confidence interval; CNS=central nervous system; CR=complete response; NE=not estimable; PR=partial response.

## SELECT SAFETY INFORMATION

**Hepatotoxicity:** Serious hepatic adverse reactions occurred in 2.1% of patients treated with GAVRETO. Increased aspartate aminotransferase (AST) occurred in 69% of patients, including Grade 3/4 in 5% and increased alanine aminotransferase (ALT) occurred in 46% of patients, including Grade 3/4 in 6%. The median time to first onset for increased AST was 15 days (range: 5 days to 1.5 years) and increased ALT was 22 days (range: 7 days to 1.7 years). Monitor AST and ALT prior to initiating GAVRETO, every 2 weeks during the first 3 months, then monthly thereafter and as clinically indicated. Withhold, reduce dose or permanently discontinue GAVRETO based on severity.

Please see additional Select Safety Information throughout, and click here to see the full [Prescribing Information](#) for GAVRETO.

# Safety of GAVRETO was evaluated in 438 patients with RET-altered tumors, including RET+ mNSCLC (n=220) and RET-altered thyroid cancer (n=138) in ARROW<sup>1</sup>

## Safety of GAVRETO in 438 patients with RET-altered tumors

- The most common adverse reactions (≥25%) were constipation, hypertension, fatigue, musculoskeletal pain and diarrhea.
- The most common Grade 3-4 laboratory abnormalities (≥2%) were decreased lymphocytes, decreased neutrophils, decreased hemoglobin, decreased phosphate, decreased calcium (corrected), decreased sodium, increased aspartate aminotransferase (AST), increased alanine aminotransferase (ALT), decreased platelets, and increased alkaline phosphatase.
- In 34 patients with RET-altered solid tumors, no large mean increase in QTc (>20 ms) was detected in the study.

## Safety of GAVRETO in RET+ mNSCLC

### Adverse reactions (≥15%) in patients who received GAVRETO in ARROW

Adverse Reactions	GAVRETO N=220	
	Grades 1-4 (%)	Grades 3-4 (%)
<b>General</b>		
Fatigue*	35	2.3**
Pyrexia	20	0
Edema†	20	0
<b>Gastrointestinal</b>		
Constipation	35	1**
Diarrhea‡	24	3.2**
Dry mouth	16	0

Adverse Reactions	GAVRETO N=220	
	Grades 1-4 (%)	Grades 3-4 (%)
<b>Musculoskeletal Disorders</b>		
Musculoskeletal pain§	32	0
<b>Vascular</b>		
Hypertension	28	14**
<b>Respiratory, thoracic, and mediastinal</b>		
Cough¶	23	0.5**
<b>Infections</b>		
Pneumonia#	17	8

\*Fatigue includes fatigue, asthenia.

†Edema includes edema peripheral, face edema, periorbital edema, eyelid edema, edema generalized, swelling.

‡Diarrhea includes diarrhea, colitis, enteritis.

§Musculoskeletal pain includes back pain, myalgia, arthralgia, pain in extremity, musculoskeletal pain, neck pain, musculoskeletal chest pain, bone pain, musculoskeletal stiffness, arthritis, spinal pain.

||Hypertension includes hypertension, blood pressure increased.

¶Cough includes cough, productive cough, upper-airway cough syndrome.

#Pneumonia includes pneumonia, atypical pneumonia, lung infection, pneumocystis jirovecii pneumonia, pneumonia bacterial, pneumonia cytomegaloviral, pneumonia haemophilus, pneumonia influenza, pneumonia streptococcal.

\*\*Only includes a Grade 3 adverse reaction.

**15% of patients permanently discontinued GAVRETO due to any adverse reaction; 6.4% discontinued due to adverse reactions considered treatment-related by the trial investigator<sup>1,3</sup>**

Adverse reactions resulting in permanent discontinuation included pneumonitis (1.8%), pneumonia (1.8%), and sepsis (1%).

### SELECT SAFETY INFORMATION

Grade ≥ 3 **hemorrhagic events** occurred in 2.5% of patients treated with GAVRETO including one patient with a fatal hemorrhagic event. Permanently discontinue GAVRETO in patients with severe or life-threatening hemorrhage.

**Tumor Lysis Syndrome (TLS):** Cases of TLS have been reported in patients with medullary thyroid carcinoma receiving GAVRETO. Patients may be at risk of TLS if they have rapidly growing tumors, a high tumor burden, renal dysfunction, or dehydration. Closely monitor patients at risk, consider appropriate prophylaxis including hydration, and treat as clinically indicated.

Please see additional **Select Safety Information** throughout, and [click here to see the full Prescribing Information](#) for GAVRETO.

# GAVRETO was generally well tolerated in mNSCLC<sup>1</sup>



## Select laboratory abnormalities (≥20%) worsening from baseline in patients who received GAVRETO in ARROW

Laboratory Abnormality*	GAVRETO N=220	
	Grades 1-4 (%)	Grades 3-4 (%)
<b>Chemistry</b>		
Increased AST	74	2.3
Increased ALT	49	2.3
Increased alkaline phosphatase	42	1.8
Decreased calcium (corrected)	39	1.8
Decreased albumin	36	0
Decreased phosphate	35	11
Increased creatinine	33	0.5
Decreased sodium	29	7
Increased potassium	26	0.9
<b>Hematology</b>		
Decreased neutrophils	61	16
Decreased hemoglobin	58	9
Decreased lymphocytes	56	19
Decreased platelets	27	3.2

\*Denominator for each laboratory parameter is based on the number of patients with a baseline and post-treatment laboratory value available, which ranged from 216 to 218 patients.

Clinically relevant laboratory abnormalities <20% of patients who received GAVRETO included hyperphosphatemia (10%).

**36%** Dose reductions due to adverse reactions in GAVRETO-treated patients

**60%** Dosage interruptions due to an adverse reaction in GAVRETO-treated patients

Adverse reactions requiring dosage reductions in ≥2% of patients included neutropenia, anemia, pneumonitis, neutrophil count decreased, fatigue, hypertension, pneumonia, and leukopenia.

Adverse reactions requiring dosage interruption in ≥2% of patients included neutropenia, pneumonitis, anemia, hypertension, pneumonia, pyrexia, increased aspartate aminotransferase (AST), increased blood creatine phosphokinase, fatigue, leukopenia, thrombocytopenia, vomiting, increased alanine aminotransferase (ALT), sepsis, and dyspnea.

# GAVRETO: the only once-daily RET inhibitor<sup>1</sup>



**Recommended starting dose: 400 mg once daily**



**Four 100-mg capsules**

Bottle and capsules are not actual size.



**Patients should take GAVRETO on an empty stomach (no food intake for at least 2 hours before and at least 1 hour after taking GAVRETO).**

Continue treatment until disease progression or until unacceptable toxicity.

If a dose of GAVRETO is missed, it can be taken as soon as possible on the same day. Resume the regular daily dose schedule for GAVRETO the next day.

Advise patients not to take an additional dose if vomiting occurs after taking GAVRETO but to continue with the next dose as scheduled.

Select patients for treatment with GAVRETO based on the presence of a RET gene fusion.

## Recommended dosage reductions for adverse reactions



**First reduction:**  
300 mg once daily



**Second reduction:**  
200 mg once daily



**Final reduction:**  
100 mg once daily

Capsules are not actual size.

Permanently discontinue GAVRETO in patients who are unable to tolerate 100 mg taken orally once daily.

## Drug Interactions

- Strong CYP3A inhibitors: Avoid coadministration.
- Combined P-gp and Strong CYP3A inhibitors: Avoid coadministration. If coadministration cannot be avoided, reduce the dose of GAVRETO as shown in Table 3 of the Prescribing Information.
- Strong CYP3A inducers: Avoid coadministration. If coadministration cannot be avoided, increase the dose of GAVRETO as shown in Section 2.5 of the Prescribing Information.

**GAVRETO is available in 100-mg capsules, giving you the opportunity to modify dosage based on individual patient needs**

## SELECT SAFETY INFORMATION

**Impaired wound healing** can occur in patients who receive drugs that inhibit the vascular endothelial growth factor (VEGF) signaling pathway. Therefore, GAVRETO has the potential to adversely affect wound healing. Withhold GAVRETO for at least 5 days prior to elective surgery. Do not administer for at least 2 weeks following major surgery and until adequate wound healing. The safety of resumption of GAVRETO after resolution of wound healing complications has not been established.

Please see additional Select Safety Information throughout, and [click here to see the full Prescribing Information](#) for GAVRETO.



## A support program for your patients

Personalized support and financial assistance for your patients taking GAVRETO

YourBlueprint™ is a patient support program designed with your patients' care in mind. YourBlueprint assists patients throughout many aspects of treatment by providing:



Financial assistance options



Temporary treatment programs



Reimbursement support

### TO ENROLL YOUR PATIENTS, VISIT US ONLINE AT



[YourBlueprint.com/HCP](https://YourBlueprint.com/HCP)



Call **1-888-BLUPRNT (1-888-258-7768)**

Monday–Friday 8AM–8PM Eastern Time (ET)

## Co-Pay Assistance Program



This program helps eligible, commercially insured patients reduce their out-of-pocket costs (co-pay, co-insurance, or deductible) to as little as \$0. For more information, see the full Terms and Conditions at [YourBlueprint.com/HCP](https://YourBlueprint.com/HCP).





## Consider GAVRETO for your next RET+ mNSCLC patient<sup>1</sup>



Selectively inhibits **RET**, a known oncogenic driver in RET+ metastatic NSCLC



**Demonstrated meaningful response** across multiple subgroups, with or without prior therapy and regardless of CNS activity at baseline



The **only once-daily** RET inhibitor



**15%** of patients permanently discontinued GAVRETO (n=220) due to any adverse reaction; **6.4%** discontinued due to adverse reactions considered treatment-related by the trial investigator<sup>1,3</sup>



In 438 patients with RET-altered solid tumors, the most common adverse reactions ( $\geq 25\%$ ) were constipation, hypertension, fatigue, musculoskeletal pain and diarrhea



The **YourBlueprint™** support program is available to help your patients throughout their treatment journey

Visit [GAVRETOhcp.com](https://GAVRETOhcp.com) to learn more or sign up for updates.

### SELECT SAFETY INFORMATION

Based on findings from animal studies and its mechanism of action, GAVRETO can cause **fetal harm** when administered to a pregnant woman. Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential to use effective non-hormonal contraception during treatment with GAVRETO and for 2 weeks after the final dose. Advise males with female partners of reproductive potential to use effective contraception during treatment with GAVRETO and for 1 week after the final dose. Advise women not to breastfeed during treatment with GAVRETO and for 1 week after the final dose.

**Common adverse reactions ( $\geq 25\%$ )** were constipation, hypertension, fatigue, musculoskeletal pain and diarrhea. **Common Grade 3/4 laboratory abnormalities ( $\geq 2\%$ )** were decreased lymphocytes, decreased neutrophils, decreased hemoglobin, decreased phosphate, decreased calcium (corrected), decreased sodium, increased AST, increased ALT, decreased platelets and increased alkaline phosphatase.

Avoid coadministration of GAVRETO with **strong CYP3A inhibitors or combined P-gp and strong CYP3A inhibitors**. If coadministration cannot be avoided, reduce the GAVRETO dose. Avoid coadministration of GAVRETO with **strong CYP3A inducers**. If coadministration cannot be avoided, increase the GAVRETO dose.

**Please see additional Select Safety Information throughout, and click here to see the full [Prescribing Information](#) for GAVRETO.**

**References:** **1.** GAVRETO™ (pralsetinib). Prescribing Information. Blueprint Medicines Corporation; Cambridge, MA. December 2020. **2.** Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Non-Small Cell Lung Cancer V.8.2020. © National Comprehensive Cancer Network, Inc. 2020. All rights reserved. Accessed September 24, 2020. To view the most recent and complete version of the guideline, go online to NCCN.org. **3.** Data on file. Blueprint Medicines Corporation. Cambridge, MA 2020.

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12/2020 USBP-PRP-20.032.4

