Breakthrough therapy designation in RET+ mNSCLC*

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

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 interstitial lung disease (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.

*Breakthrough Therapy designation for the treatment of patients with RET fusion+ non–small cell lung cancer that has progressed following platinum-based chemotherapy.

GAVRETO was studied in both treatment-naive and previously platinum-treated NSCLC patients[1]

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+ 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[1,2]

	Treatment-naive patients (n=27)	Previously platinum-treated patients (n=87)
Median age	65 years (30-87)	60 years (28-85)
Gender	52% female 48% male	49% female 51% male
Race/ethnicity	59% White, 33% Asian, 4% Hispanic/Latino	53% White, 35% Asian, 6% Hispanic/Latino
ECOG status	0-1: 96% 2: 4%	0-1: 94% 2: 6%
RET fusion partner	70% KIF5B 11% CCDC6	75% KIF5B 17% CCDC6
Brain metastases at baseline	37%	43%
Prior therapy	Per protocol, patients were not eligible for platinum-based chemotherapy based on investigator assessment[2]	45% PD-1/PD-L1 inhibitor, 25% prior kinase inhibitors
Patient identification	67% NGS • 41% tumor samples • 22% blood or plasma • 4% unknown 33% FISH	77% NGS • 45% tumor samples • 26% blood or plasma • 6% unknown 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; RECIST=Response Evaluation Criteria in Solid Tumors.

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.

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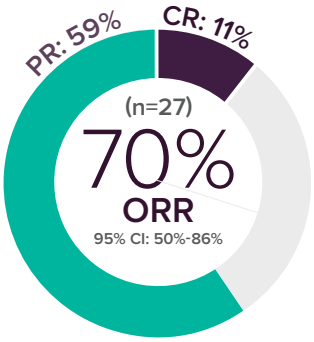
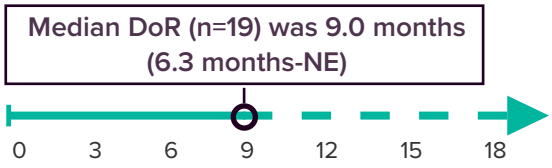
GAVRETO demonstrated robust and durable response with or without prior therapy[1]

Efficacy results with GAVRETO[1,2]

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.

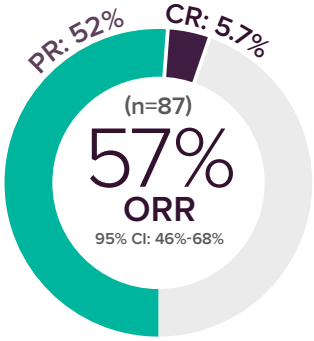
TREATMENT-NAIVE PATIENTS

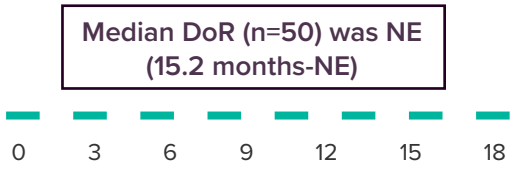




- 58% of patients continued to respond to treatment at 6 months*
- Median time to first response was 1.9 months (range: 1.4-5.6 months)[2]

PREVIOUSLY PLATINUM-TREATED PATIENTS





- 80% of patients continued to respond to treatment at 6 months*
- Median time to first response was 1.8 months (range: 1.3-9.1 months)[2]

GAVRETO demonstrated consistent response across previously platinum-treated subgroups[1,2]

CNS ACTIVITY

Brain metastases at baseline (n=8): 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)

RET PARTNER[2] | Exploratory analysis

KIF5B (n=65): 59% ORR (95% CI: 46%-71%)

CCDC6 (n=15): 60% ORR (95% CI: 32%-84%)

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

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

GAVRETO™ pralsetinib

Safety of GAVRETO was evaluated in 220 patients with RET+ mNSCLC in ARROW[1]

- The most common adverse reactions (≥25%) were fatigue, constipation, musculoskeletal pain, and hypertension
- The most frequent serious adverse reaction (in ≥2% of patients) was pneumonia, pneumonitis, sepsis, urinary tract infection, and pyrexia
- Fatal adverse reaction occurred in 5% of patients; fatal adverse reaction which occurred in >1 patient included pneumonia (n=3) and sepsis (n=2)

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

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

Adverse Reactions	GAVRETO N=220	
	Grades 1-4 (%)	Grades 3-4 (%)
Musculoskeletal Disorders		
Musculoskeletal pain§	32	0
Vascular		
Hypertension‖	28	14**
Respiratory, thoracic, and mediastinal		
Cough¶	23	0.5**
Infections		
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.

94.5% of patients did not discontinue GAVRETO due to treatment-related adverse reactions.[2]

85% of patients did not discontinue GAVRETO due to any adverse reaction.

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

SELECT SAFETY INFORMATION

Hepatotoxicity: Serious hepatic adverse reactions occurred in 2.1% of patients treated with GAVRETO. Increased AST occurred in 69% of patients, including Grade 3/4 in 5.4% and increased 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.

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.

Please see additional Select Safety Information throughout, and click here to see the full Prescribing Information for GAVRETO.

GAVRETO was generally well tolerated[1]

The most common Grade 3-4 laboratory abnormalities (≥2%) were decreased lymphocytes, decreased neutrophils, decreased phosphate, decreased hemoglobin, decreased sodium, decreased calcium (corrected), and increased alanine aminotransferase (ALT).

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 (%)
Chemistry		
Increased aspartate aminotransferase (AST)	69	1.1
Increased alanine aminotransferase (ALT)	46	2.1
Increased creatinine	42	1.1
Increased alkaline phosphatase	40	1.1
Decreased calcium (corrected)	29	2.2
Decreased sodium	27	3.2
Decreased phosphate	27	9
Hematology		
Decreased hemoglobin	54	5
Decreased lymphocytes	52	20
Decreased neutrophils	52	10
Decreased platelets	26	0

*Denominator for each laboratory parameter is based on the number of patients with a baseline and post-treatment laboratory value available, which ranged from 83 to 94 patients.

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

In 34 patients with RET fusion–positive solid tumors, no large mean increase in QTc (>20 ms) was detected in the study.

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™ pralsetinib

GAVRETO: the only once-daily RET inhibitor[1]

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.

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.

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.

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
- Prior authorization and appeals support
- Benefits investigation

TO ENROLL YOUR PATIENTS, VISIT US ONLINE AT

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.

GAVRETO™ pralsetinib

GAVRETO™
pralsetinib

Consider GAVRETO for your next RET+ mNSCLC patient[1]

- 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
- **94.5%** of patients did not discontinue GAVRETO due to treatment-related adverse reactions[2]
  85% of patients did not discontinue GAVRETO due to any adverse reaction
- The most common adverse reactions (≥25%) were fatigue, constipation, musculoskeletal pain, and hypertension
- The **YourBlueprint**™ support program is available to help your patients throughout their treatment journey

Visit GAVRETOhcp.com/NowApproved
to learn more or sign up for updates.

SELECT SAFETY INFORMATION

Common adverse reactions (≥25%) were fatigue, constipation, musculoskeletal pain, and hypertension. **Common Grade 3-4 laboratory abnormalities (≥2%)** were decreased lymphocytes, decreased neutrophils, decreased phosphate, decreased hemoglobin, decreased sodium, decreased calcium (corrected) and increased alanine aminotransferase (ALT).

Avoid coadministration with **strong CYP3A inhibitors.** Avoid coadministration of GAVRETO with **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. September 2020.
2. Data on file. Blueprint Medicines Corporation. Cambridge, MA 2020.

09/2020 USBP-PRP-20.032.2

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