Sustained Biochemical Efficacy and Safety of Seladelpar in Patients with Primary Biliary Cholangitis, Including Those at High Risk for Progression, up to 5 Years of Treatment from ASSURE

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Conclusions

- Seladelpar led to sustained improvements in biochemical markers of cholestasis, including among primary biliary cholangitis (PBC) patients with high risk of disease progression
- Seladelpar was well tolerated with a consistent safety profile and no new safety signals identified with up to 5 years of treatment
- Long-term seladelpar treatment led to sustained reductions in pruritus among patients with moderate to severe pruritus at baseline
- Sample size for the LSM ≥10 kPa subpopulation was small at Month 48, thus, results should be interpreted with caution; this study is ongoing

Plain Language Summary

- In this study of people with primary biliary cholangitis (PBC), seladelpar treatment reduced disease activity, even for people at high risk for worsening disease
- People treated with seladelpar also had lasting improvements in itch, a bothersome symptom common in PBC
- People receiving seladelpar in this study did not experience serious side effects related to the treatment

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Introduction

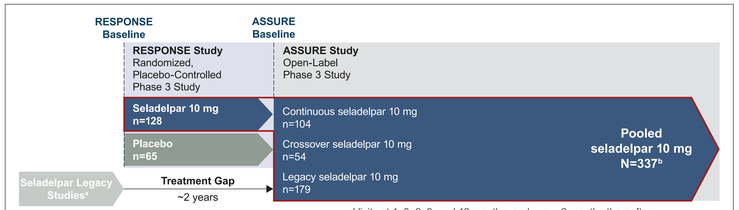
- Primary biliary cholangitis (PBC) is a chronic, slowly progressive disease characterized by a high symptom burden (e.g., pruritus) and the need for long-term therapy, underscoring the importance of sustained efficacy and safety of treatment options[1]
- Younger age at diagnosis and advanced liver fibrosis are factors associated with increased risk of PBC progression;[2–4] evaluation of the efficacy and safety of PBC therapies in high-risk patients, alongside the broader patient population, is essential to inform clinical practice
- Many patients with PBC receiving ursodeoxycholic acid (UDCA) treatment, who have an inadequate response, are at increased risk of developing cirrhosis and eventual hepatic decompensation[5]
- Seladelpar is a first-in-class delpar (selective peroxisome proliferator-activated receptor delta [PPARδ] agonist) indicated for the treatment of PBC in combination with UDCA in adults who have an inadequate response to UDCA or as monotherapy in patients who are unable to tolerate UDCA[6–9]
- In the pivotal, placebo-controlled, Phase 3 RESPONSE trial (NCT04620733), seladelpar significantly reduced alkaline phosphatase (ALP) levels, a key marker of PBC disease activity, compared with placebo, and significantly improved pruritus in patients with moderate to severe pruritus[6]
- The ongoing, open-label, Phase 3 ASSURE study (NCT03301506)[10] evaluates the long-term efficacy and safety of seladelpar in patients with PBC, both in the overall study population and in subpopulations at high risk of disease progression and/or with substantial symptom burden (e.g., pruritus)

Objective

- To report the progress on the long-term efficacy and safety of seladelpar treatment up to 5 years in patients with PBC, including subpopulations at high risk for disease progression and those with clinically significant pruritus

Methods

Figure 1. Study Design



Data cutoff: January 31, 2026.
[a]Phase 2 dose-ranging study (NCT02955602), Phase 3 long-term safety study (NCT03301506), Phase 3 ENHANCE study (NCY03602560), Phase 1b hepatic impairment study (NCT04950764). The Phase 2 and 3 parent studies required inadequate response or intolerance to first-line UDCA. [b]The red outline indicates the pooled population in ASSURE (NCT03301506) of patients who received 10 mg seladelpar. For patients who started seladelpar in RESPONSE (NCT04620733), that exposure time is included in the ASSURE pooled analysis. Two patients initiated seladelpar at 5 mg and were excluded from the analysis.
N, overall population; n, population by parent study; UDCA, ursodeoxycholic acid.

Seladelpar Treatment Duration at Data Cutoff

	Year 1	Year 2	Year 3	Year 4	Year 5
Patients who completed treatment through time point, n (%)	325 (96)	298 (88)	243 (72)	116 (34)	2 (<1)

- Patients rolled over directly from RESPONSE or enrolled after prior participation in a legacy study and received open label seladelpar 10 mg daily in ASSURE (**Figure 1**)
- This analysis is based on a pooled population of all patients enrolled in ASSURE where baseline was defined as the time of seladelpar initiation in RESPONSE or ASSURE. The data cutoff for this interim analysis was January 31, 2026
- High-risk subpopulations were defined as patients aged ≤62 years and/or with liver stiffness measurement (LSM) ≥10 kPa at baseline
- Efficacy endpoints included ALP percent change from baseline through Month 48, the latest time point with N >100 patients, assessed in the overall study population as well as in high-risk subpopulations
  - Attainment of ALP normalization (defined as ALP ≤1 × upper limit of normal [ULN]) was assessed in the overall study population at each study visit
- Clinically meaningful improvement in pruritus numerical rating scale (NRS), defined as ≥3-point reduction, was assessed in patients with moderate to severe pruritus at baseline (NRS values of ≥4)
- Patients who had PBC-related clinical outcomes (death, liver transplantation, Model for End-Stage Liver Disease score ≥15 for at least 2 consecutive visits, ascites requiring treatment, hospitalization for decompensation event [esophageal varices hemorrhage, spontaneous bacterial peritonitis, hepatic encephalopathy]) or who met liver safety criteria that led to seladelpar discontinuation (i.e., intercurrent events) were considered non-responders for all subsequent time points
- Safety was assessed by patient incidence of adverse events (AEs) adjusted for exposure time using all available data through Month 60 in this interim analysis

Results

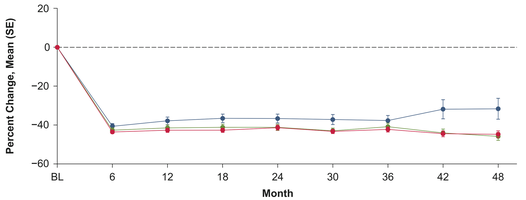
Table 1. Demographics and Baseline Characteristics

	SEL 10 mg (N=337)
Age at screening, years, mean (SD)	58 (9.7)
Age group at screening, years, n (%)	
≤62	218 (64.7)
>62	119 (35.3)
Sex, female, n (%)	318 (94.4)
Race, n (%)	
White	291 (86.4)
Asian	24 (7.1)
Body mass index, kg/m², mean (SD)	27.3 (5.8)
On UDCA, n (%)	320 (95.0)
Cirrhosis, n (%)	52 (15.4)
Child-Pugh A, n (%)[a]	48 (92.3)
Liver stiffness, kPa, mean (SD)	10.0 (8.1)
Liver stiffness ≥10 kPa, n (%)	104 (30.9)
ALP, U/L,[b] mean (SD)	287 (128.2)
AST, U/L,[b] mean (SD)	38 (16.3)
ALT, U/L,[b] mean (SD)	43 (23.0)
GGT, U/L,[b] mean (SD)	235 (211.5)
TB, mg/dL,[b] mean (SD)	0.8 (0.3)
Pruritus NRS, mean (SD)	2.8 (2.8)
Patients with moderate to severe pruritus,[c] n (%)	108 (32.0)

ASSURE data cutoff: January 31, 2026. [a]Percentage out of patients with cirrhosis. [b]ALP ULN=116 U/L; AST ULN=34 U/L; ALT ULN=41 U/L; GGT ULN=52 U/L for male patients, 38 U/L for female patients;[c] TB ULN=1.10 mg/dL.[10] [c]Defined as pruritus NRS ≥4.
ALP, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; GGT, gamma-glutamyl transferase; NRS, numerical rating scale; SD, standard deviation; SEL, seladelpar; TB, total bilirubin; UDCA, ursodeoxycholic acid; ULN, upper limit of normal.

- Of the total, 218/337 (64.7%) patients were aged ≤62 years, 104/337 (30.9%) patients had LSM ≥10 kPa, and 108/337 (32.0%) had moderate to severe pruritus at baseline (**Table 1**)
- Patients in high-risk subpopulations had higher ALP at baseline compared with the overall population (298 U/L [aged ≤62 years] and 308 U/L [LSM ≥10 kPa] versus 287 U/L [overall]); the LSM ≥10 kPa subpopulation also had higher rates of cirrhosis (42.3%) versus the overall population (15.4%)
  - Of the patients aged ≤62 years or with LSM ≥10 kPa, 77/218 (35.3%) and 48/104 (46.2%) had moderate to severe pruritus, respectively, at baseline
- Among the 337 patients included, 242 (71.8%) and 109 (32.3%) received seladelpar for ≥36 and ≥48 months, respectively, as of the data cutoff

Figure 2. Percent Change from Baseline in ALP Through 48 Months of Seladelpar Treatment, Overall and in High-Risk Subpopulations

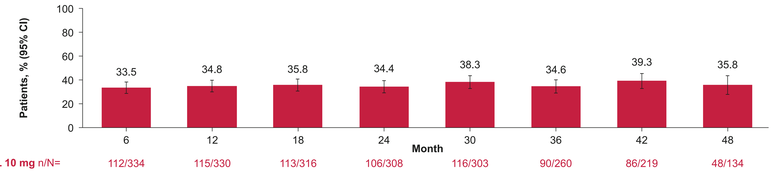


	BL	6	12	18	24	30	36	42	48
Overall SEL 10 mg n=	332	325	311	298	288	243	202	116	
Age ≤62 years n=	214	211	197	189	180	154	129	71	
LSM ≥10 kPa n=	101	96	94	86	80	65	48	28	

ASSURE data cutoff: January 31, 2026. n = number of evaluable patients at each time point.
ALP, alkaline phosphatase; LSM, liver stiffness measurement; SE, standard error; SEL, seladelpar.

- In the overall population, seladelpar led to sustained ALP reductions, with a mean (SE) ALP change from baseline of −44.7% (1.9) at Month 48 (**Figure 2**)
  - Among high-risk individuals, mean (SE) ALP change from baseline was −45.8% (2.2) in the ≤62-year subpopulation and −31.6% (5.5) in the LSM ≥10 kPa subpopulation, at Month 48

Figure 3. Proportion of Patients Attaining ALP Normalization Through 48 Months of Seladelpar Treatment

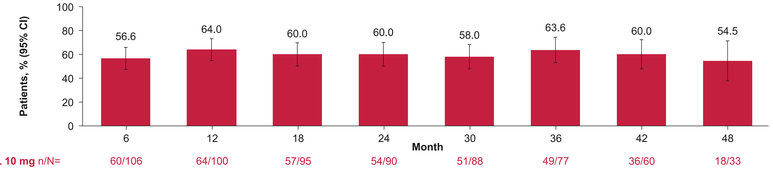


	6	12	18	24	30	36	42	48
SEL 10 mg n/N=	112/334	115/330	113/316	106/308	116/303	90/260	86/219	48/134

ASSURE data cutoff: January 31, 2026. ALP normalization was defined as ALP ≤1 × ULN. n/N = number of responders/number of evaluable patients at each time point.
ALP, alkaline phosphatase; CI, confidence interval; SEL, seladelpar; ULN, upper limit of normal.

- In the overall population, the percentage of patients attaining ALP normalization ranged from 33.5% (112/334) to 39.3% (86/219) across time points, with 35.8% (48/134) attaining ALP normalization at Month 48 (**Figure 3**)
  - Among high-risk subpopulations, at Month 48, ALP normalization was attained by 31.7% (26/82) of patients aged ≤62 years at study entry and 9.5% (4/42) of patients with LSM ≥10 kPa at entry

Figure 4. Proportion of Patients Attaining ≥3-Point Improvement in Pruritus NRS Through 48 Months of Seladelpar Treatment



	6	12	18	24	30	36	42	48
SEL 10 mg n/N=	60/106	64/100	57/95	54/90	51/88	49/77	36/60	18/33

ASSURE data cutoff: January 31, 2026. n/N = number of responders/number of evaluable patients with moderate to severe pruritus. Moderate to severe pruritus was defined as baseline pruritus NRS ≥4.
CI, confidence interval; NRS, numerical rating scale; SEL, seladelpar.

- In patients with moderate to severe pruritus at baseline, over half attained an NRS change of −3.0 at all time points (54.5% [18/33] at Month 48; **Figure 4**)

Table 2. Overall Exposure-Adjusted Safety Outcomes Per 100 Patient-Years

n (n/E × 100)	SEL 10 mg					
	Overall (N=337) (E=1147.2 years)	Year 1 (N=337) (E=331.0 years)	Year 2 (N=326) (E=307.6 years)	Year 3 (N=299) (E=274.4 years)	Year 4 (N=244) (E=187.7 years)	Year 5 (N=118) (E=46.4 years)
Any AE (at least one)	327 (28.5)	278 (84.0)	231 (75.1)	212 (77.3)	134 (71.4)	22 (47.4)
Serious AE[a]	79 (6.9)	26 (7.9)	21 (6.8)	28 (10.2)	16 (8.5)	1 (2.2)
Treatment-related serious AE	0	0	0	0	0	0
Grade 3 or higher AE	88 (7.7)	32 (9.7)	30 (9.8)	32 (11.7)	13 (6.9)	1 (2.2)
AE with action taken as permanent withdrawal of study drug	40 (3.5)	7 (2.1)	17 (5.5)	11 (4.0)	5 (2.7)	0
AE leading to death[b]	3 (0.3)	0	1 (0.3)	0	2 (1.1)	0

ASSURE data cutoff: January 31, 2026. All AEs listed were treatment-emergent. For participants who initiated seladelpar 10 mg in ASSURE, data up to Month 12 for Year 1, after Month 12 through Month 24 for Year 2, after Month 24 through Month 36 for Year 3, after Month 36 through Month 48 for Year 4, and after Month 48 through Month 60 for Year 5 are included. For participants who rolled over from the RESPONSE seladelpar arm, RESPONSE data for Year 1, ASSURE data up to Month 12 for Year 2, after Month 12 through Month 24 for Year 3, after Month 24 through Month 36 for Year 4, and after Month 36 through Month 48 for Year 5 are included. Adverse events were coded using MedDRA version 28.1, and severity grades were defined by CTCAE Version 5.0. [a]Serious AEs adjudicated as PBC clinical outcomes were esophageal varices hemorrhage, autoimmune hemolytic anemia, intracranial hemorrhage, metastatic lung cancer, and pneumonia. [b]The three adverse events leading to death included autoimmune hemolytic anemia, metastatic lung cancer, and an intracranial hemorrhage associated with a head injury. All events were assessed by the Investigators as not related to seladelpar.
AE, adverse event; CTCAE, Common Terminology Criteria for Adverse Events; E, sum of seladelpar exposure in years; MedDRA, Medical Dictionary for Regulatory Activities; PBC, primary biliary cholangitis; SEL, seladelpar.

- No treatment-related serious AEs were reported through Month 60 of seladelpar exposure (**Table 2**)
  - As of the data cutoff, 15/337 patients (4.5%) experienced a PBC-related clinical outcome