CYMABAY THERAPEUTICS

Improving the Lives of Patients with Liver Diseases

Corporate Presentation

November 2019

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CymaBay
Transforming into a fully integrated company

CymaBay

- Focus on improving the lives of patients with inflammatory liver diseases
- Targeting indications with limited or no approved therapies and high unmet need
- Forward integrating into a Commercial organization to prepare for first launch

Seladelpar

- Poised to be the first and only selective PPARδ agonist approved for patients
- Potent PPARδ agonist with pleiotropic regulation of critical liver disease pathways
- Oral once daily dose with advantageous tolerability profile

Value

- Three late-stage development programs reading out in the next 2 years
- Highly de-risked pivotal Phase 3 in Primary Biliary Cholangitis (PBC) with Breakthrough Therapy Designation (BTD)
- Phase 2 initiated in Primary Sclerosing Cholangitis (PSC), a second orphan cholestatic liver disease
- NASH Phase 2b presents upside and strategic options

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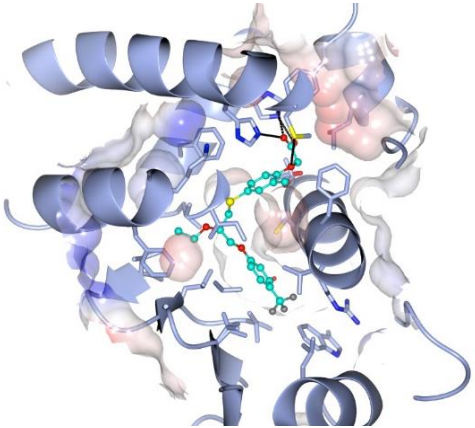
CymaBay
Delivering on seladelpar to drive value

Seladelpar
Differentiated opportunity addressing unmet needs in liver disease



1.8 Å RMSD X-ray Crystal Structure Seladelpar - PPARδ Ligand Binding Domain
EC_{50} = 2nM

- First potent and selective PPARδ agonist in development for inflammatory liver diseases
- Oral, once daily with clinical activity down to 5 mg and clinical experience with exposures beyond one year
- Regulation of pathways important in inflammatory liver diseases; bile acids, lipid metabolism, inflammation and fibrosis

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Seladelpar

Targets all important cell types in liver disease

Decrease Bile Acids

Hepatocyte

Cholangiocyte

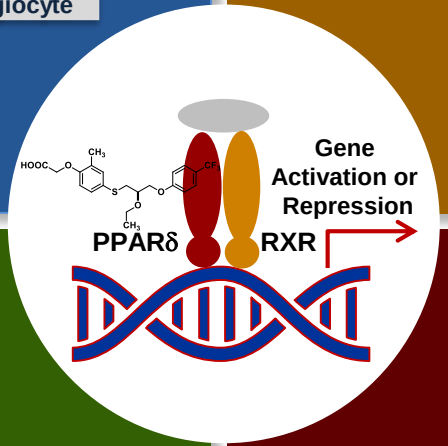
- ↓ Cholesterol synthesis
- ↓ Bile acid synthesis (C4)
- ↑ Transport

Anti-Inflammatory

Kupffer Cell

Macrophage

- ↓ NFκB-dependent gene activation
- ↓ Inflammatory cytokines
- ↓ hs-C-Reactive Protein



Anti-Fibrotic

- ↓ Connective Tissue Growth Factor
- ↓ Stellate cell activation
- ↓ Collagen synthesis/deposition

Stellate Cell

Increase Lipid Metabolism

- ↓ Cholesterol/LDL-C
- ↑ Fatty acid oxidation
- ↑ Insulin sensitivity

Hepatocyte

Myocyte

Adipocyte

Enterocyte

Regulates genes that control pathways in liver health and disease

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Seladelpar
Primary Biliary Cholangitis

Breakthrough Therapy (FDA) and

Priority Medicine (EMA) Designations

Potential to serve the two key unmet needs for patients with PBC –

better efficacy and improved tolerability

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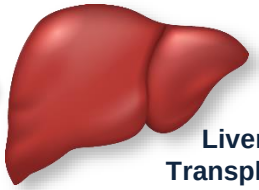
Primary Biliary Cholangitis

Orphan, autoimmune inflammatory disease of the liver

Cholestasis → Fibrosis → Cirrhosis



Liver Transplant

- Impairment of bile flow (cholestasis), portal inflammation and destruction of bile ducts
- Elevated serum markers of cholestasis including alkaline phosphatase (AP), gamma-glutamyl transferase (GGT) and total bilirubin
- Clinical symptoms of fatigue and pruritus (itching)
- Affects 1 in 1,000 women over 40 (~130,000 patients in the U.S.)

AP below 1.67x the upper limit of normal and normal total bilirubin are clinical surrogates for slowing disease progression

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Despite Current Therapies Unmet Need Remains

Patients need improved efficacy and better tolerability

Ursodeoxycholic Acid (UDCA)
1st Line

- ▲First line therapy for PBC
- ▼~40% inadequate responders: AP >1.67x ULN
- ▼Additional 5% are intolerant to therapy

Obeticholic Acid (Ocaliva)
2nd Line

- ▲Add-on therapy for UDCA inadequate responders
- ▲Monotherapy for UDCA intolerant patients
- ▲AP/bilirubin as biomarkers for accelerated approval
- ▼~50% inadequate responders
- ▼Can cause or worsen pruritus

Seladelpar is being developed as a potential improved 2nd line treatment for PBC

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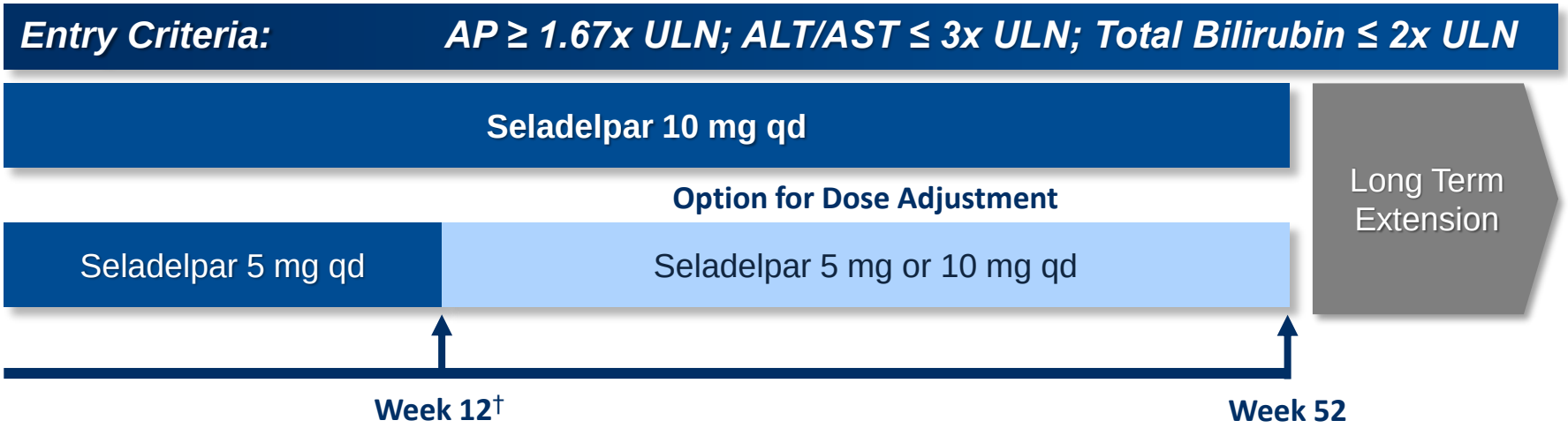
Seladelpar Phase 2 Open Label Study in PBC

Add-on for patients with an inadequate response or intolerance to UDCA



Primary Outcome: *% change in AP from baseline*

Secondary Outcomes: *composite responder rate‡, AP normalization, changes in liver, metabolic and inflammatory markers*

†At week 12 a dose adjustment in the 5/10 mg group was made based on patient response and tolerability.
‡Patients with AP≤1.67x ULN, ≥15% drop in AP from baseline and normal total bilirubin.

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Seladelpar Phase 2 Study in PBC
*Baseline demographics of mITT population (N=34 at 52 weeks)**

Parameters Mean (SD) (Reference Range)	Seladelpar 5/10 mg (n=17)	Seladelpar 10 mg (n=17)
Age, years	49 (5)	48 (11)
Female/male	17/0	16/1
History of Pruritus, n (%)	11 (65)	14 (82)
Pruritus VAS (0-100)	19 (22)	37 (31)
AP (37-116 U/L)	351 (166)	279 (74)
ALT (6-41 U/L)	41 (17)	52 (25)
Total bilirubin† (0.10-1.10 mg/dL)	0.56 [0.50, 0.70]	0.75 [0.57, 1.14]
UDCA Dose, mg/kg/day	15 (4)	17 (3)

*Data as of July 23, 2018 and includes only patients that reached 52-weeks at such date
†Median [Quartiles: 25, 75]. mITT, modified intention to treat; VAS, visual analogue scale.

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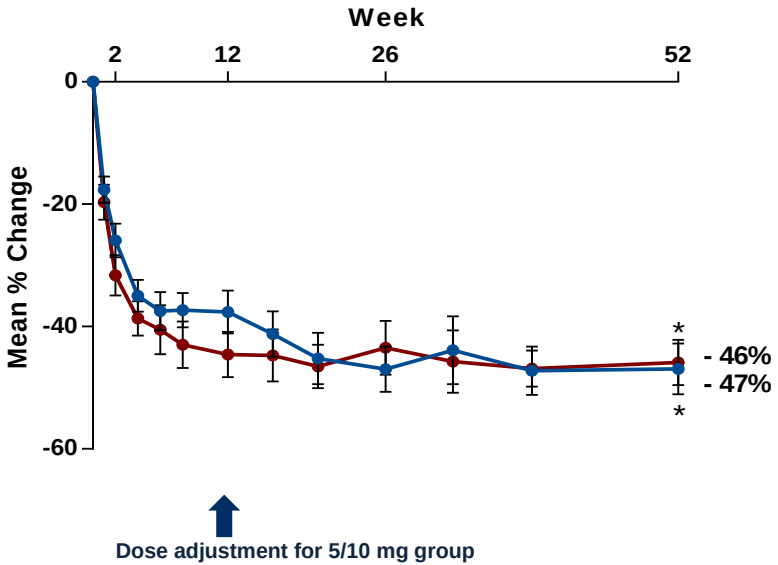
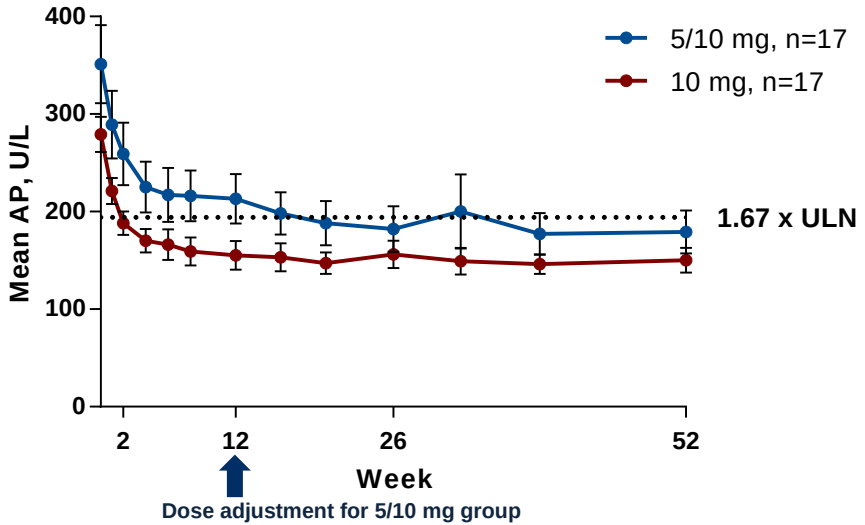
Seladelpar Phase 2 Study in PBC

Rapid and sustained decrease in AP through week 52

Mean Percent AP Change Baseline to Week 52



Mean AP from Baseline to Week 52



Decreases in AP >45% observed at 5/10 mg and 10 mg

*P<0.0001 for both groups compared to baseline values
Mean ± SEM

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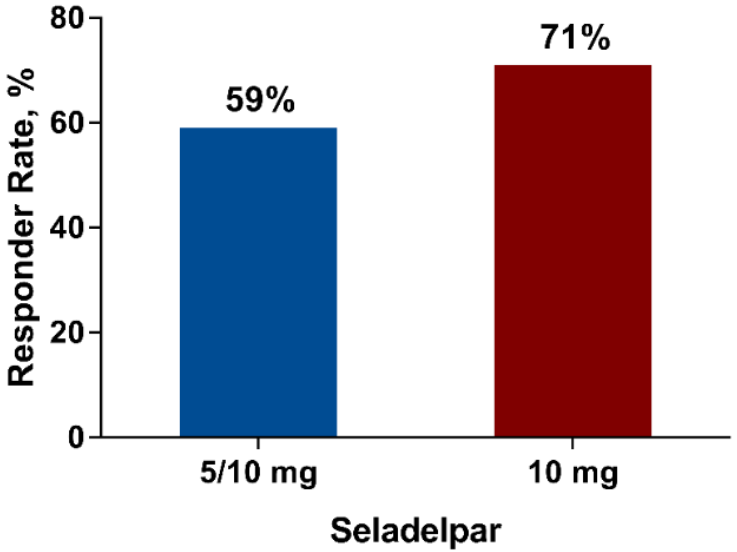
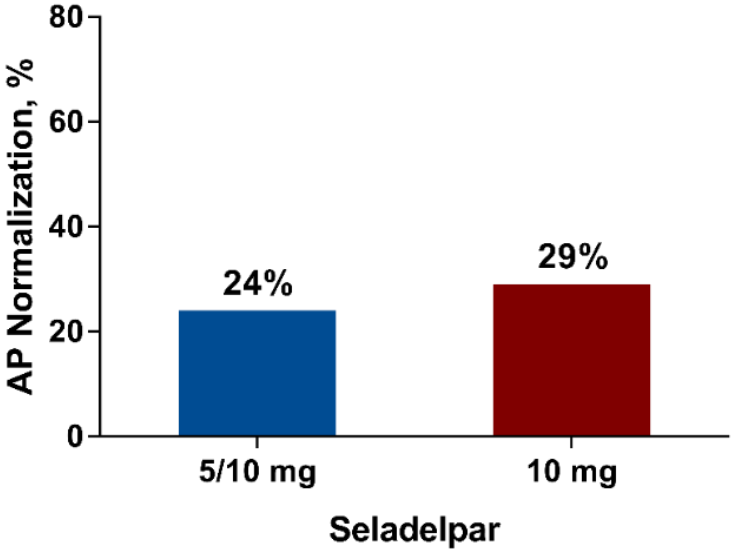
Seladelpar Phase 2 Study in PBC

Up to 71% of patients achieved the composite efficacy endpoint

Composite Responder Rate



AP Normalization



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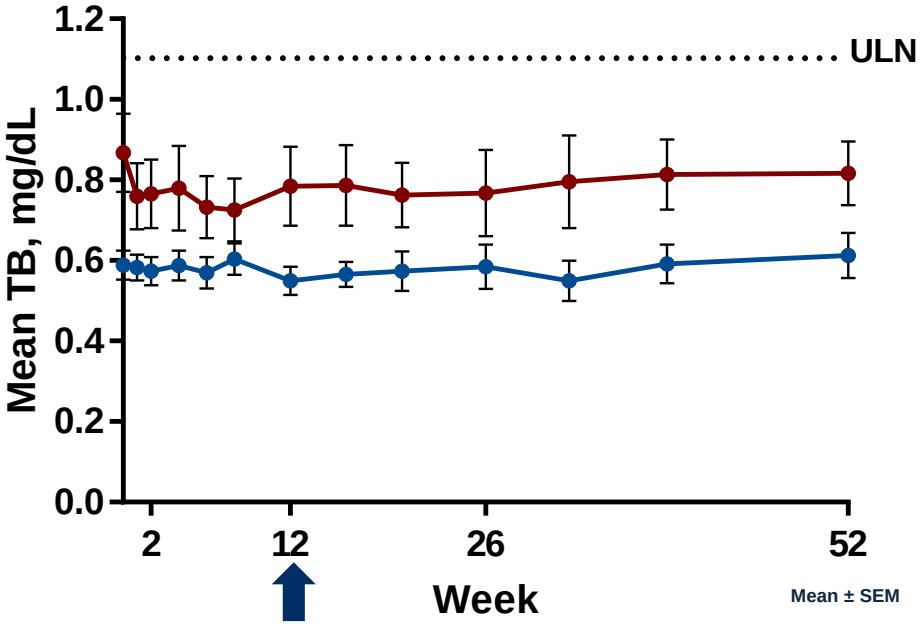
Seladelpar Phase 2 Study in PBC

Average total bilirubin levels stable through week 52

Mean Total Bilirubin

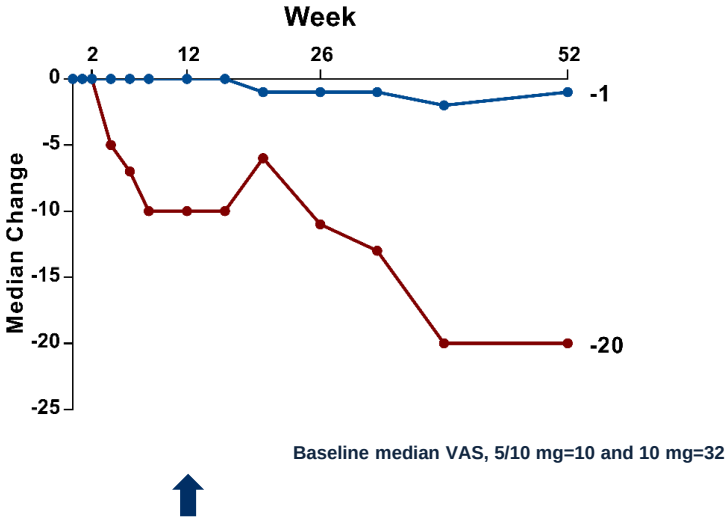


Dose adjustment for 5/10 mg group

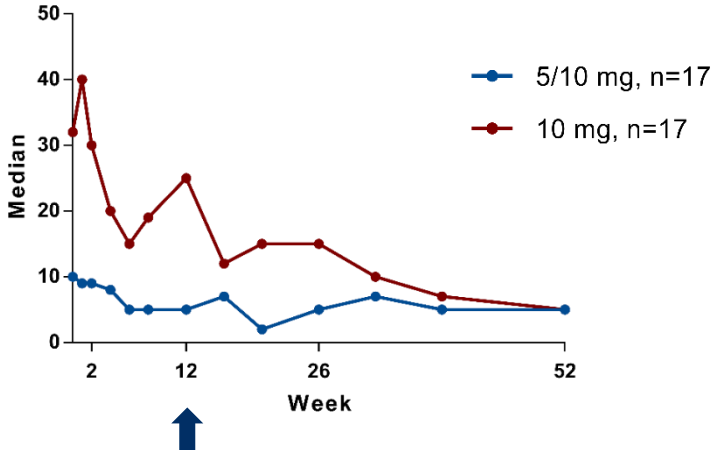
Seladelpar Phase 2 Study in PBC
Patient reported pruritus: Treatment not associated with increase

Visual Analog Scale (VAS) through week 52

Median Change in VAS



Median VAS



- In patients with baseline itch, the median changes in VAS were -30% and -66% in the 5/10 mg and 10 mg groups, respectively

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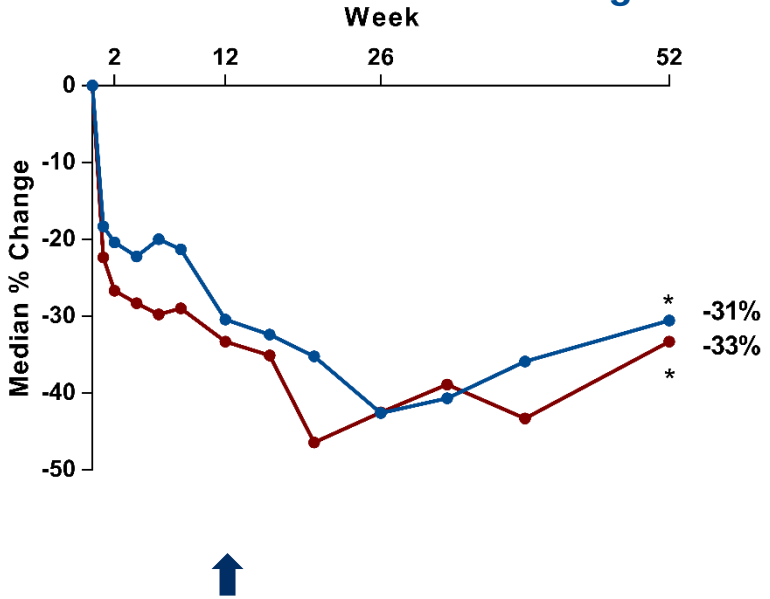
Seladelpar Phase 2 Study in PBC

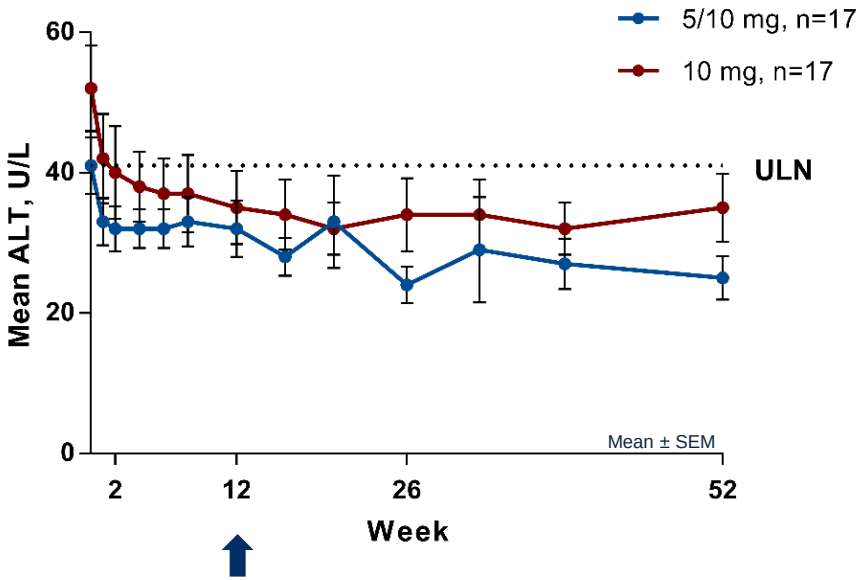
Significant decreases in transaminase through week 52

Median Percent ALT Change



Dose adjustment for 5/10 mg group

Mean ALT



Dose adjustment for 5/10 mg group

*P<0.0001, compared to baseline values

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Seladelpar Phase 2 Study in PBC
Safety summary (n=119)

- 11 serious AEs in the study; none were deemed related to seladelpar
- No ≥ grade 3 ALT elevations
- Three discontinuations
  - Related: Grade 1 gastroesophageal reflux
  - Unrelated: Pneumonia & worsening of pruritus
- No discontinuations for transaminase elevations
- Overall, no increase in pruritus

Most Common AEs

AE	5/10 mg	10 mg
Pruritus	22%	18%
Fatigue	13%	7%
Diarrhea	14%	6%
Nausea	14%	6%

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Seladelpar for PBC
Significantly de-risked Phase 3 program

Response of up to 71% of patients in registration endpoint

No signal for drug-induced itch

Phase 2 study enrolled with 104 patients beyond 52 weeks

ENHANCE Phase 3 global registration study enrolling

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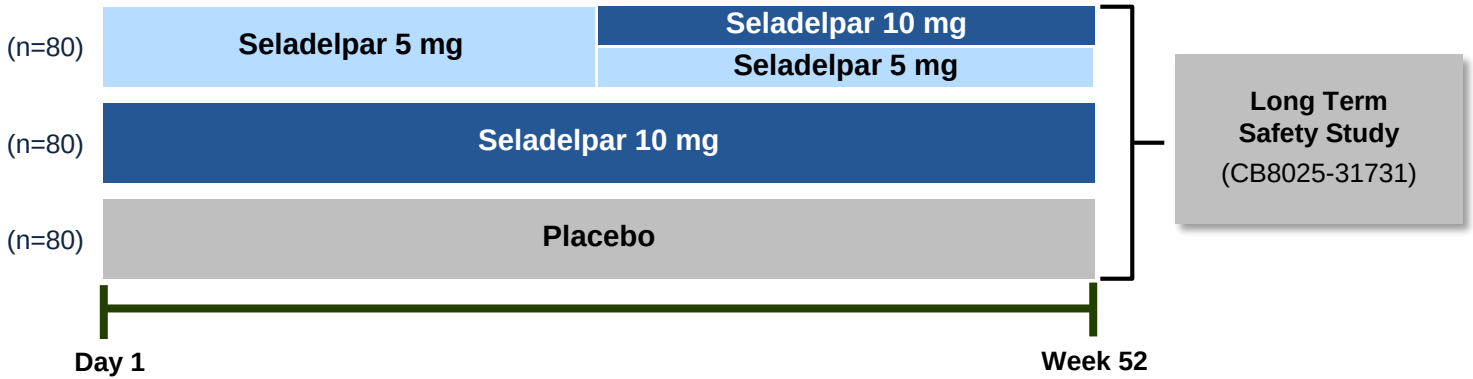
ENHANCE Phase 3 Pivotal Study

Phase 3 study design

ENHANCE
A study of Primary Biliary Cholangitis

n=240 (80/group)



Primary Outcome: Composite responder rate (AP <1.67xULN, ≥15% decrease in AP, total bilirubin ≤ULN)

Secondary Outcomes: Proportion of patients with AP ≤1.0xULN at 6 and 12 months
Change from baseline in pruritus Numerical Rating Scale using e-diary at 6 months

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ENHANCE Phase 3 Pivotal Study
Same population, dose and endpoint as Phase 2 study

Population	▪ Intolerance or inadequate response to UDCA ▪ AP ≥ 1.67 x ULN, bilirubin ≤ 2 x ULN ▪ Includes patients with severe pruritus
Design	▪ Double blind, 52-week, placebo-controlled ▪ Seladelpar 5/10 mg titration and 10 mg vs. placebo (1:1:1 randomization) ▪ Stratified by AP and pruritus
Primary Outcome	▪ Composite responder rate (AP <1.67xULN, ≥15% decrease in AP, total bilirubin ≤ULN)
Secondary Outcomes	▪ Proportion of patients with AP ≤1.0xULN at 6 and 12 months ▪ Change from baseline in pruritus Numerical Rating Scale using e-diary at 6 months

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Primary Sclerosing Cholangitis(PSC)

Anti-cholestatic and Anti-inflammatory Activities that May Support Potential Treatment Effect in PSC

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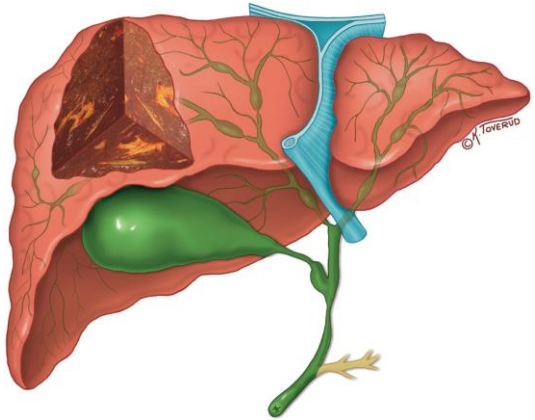
Primary Sclerosing Cholangitis

Orphan, cholestatic inflammatory disease of the liver

- Characterized by diffuse inflammation and fibrosis of both intra- and extra-hepatic bile ducts
- May progress to end-stage liver disease
- Common initial symptoms are fatigue, abdominal pain and itching (pruritus)
- ~ 70% of patients have IBD
- Cholangiocarcinoma develops in 8–30% of patients
- Affects men 2:1 (~40,000 patients in the U.S.)



Hirschfield, et al; The Lancet. 2013

Only effective therapy is liver transplant

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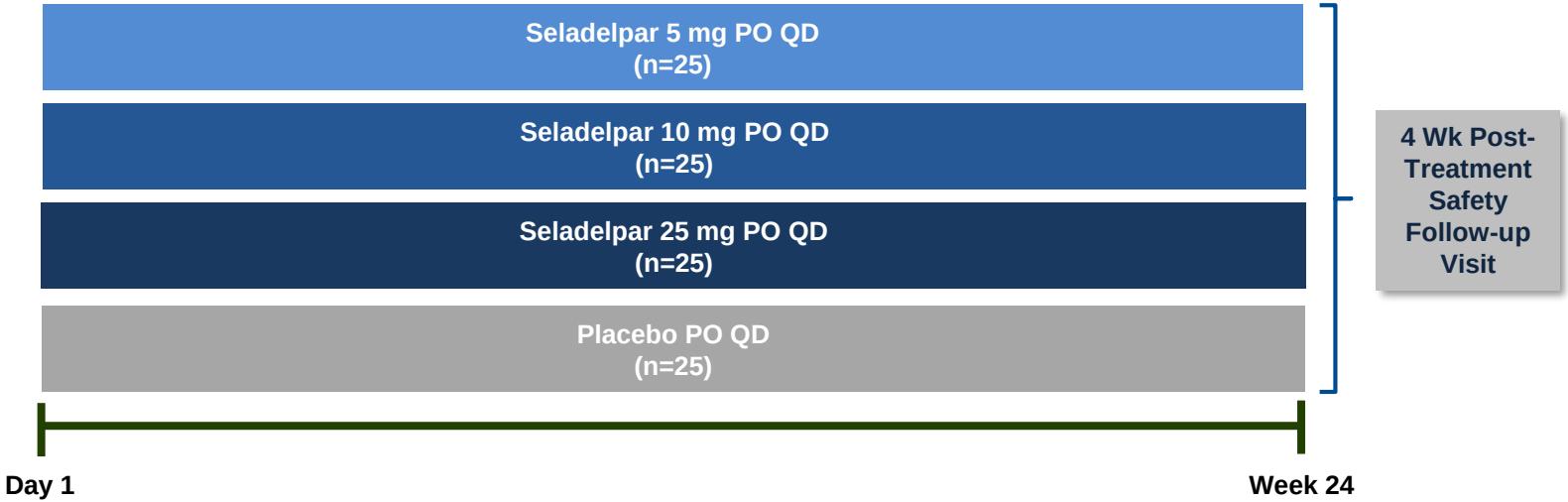
Seladelpar PSC
24 -Week Phase 2 study design



Primary Outcome: *% change in AP from baseline to week 24*

Secondary Outcomes: *FibroScan, MRCP and other exploratory measures*

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Non-alcoholic Steatohepatitis (NASH)

Potential mechanism that decreases disease drivers of NASH:

- *metabolic load – reduces bile acids, cholesterol & lipids*
- *cell stress and injury – reverses hepatocellular ballooning*
- *inflammation and fibrosis – lowers macrophages & collagen*

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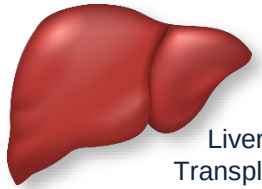
Seladelpar for NASH

Potential role for PPARδ agonists in the treatment of NASH

Metabolic Load → Cell Stress & Injury → Inflammation → Fibrosis → Liver Transplant



Pathological Progression from NAFLD to NASH

▪ Steatosis ▪ Insulin resistance ▪ Bile acids ▪ Free Cholesterol ▪ Lipotoxic lipids	▪ ER stress/ROS ▪ Inflammatory mediators	▪ Activation & recruitment - Kupffer cells - macrophages - neutrophils ▪ Cell death ▪ Stellate cell activation	▪ Extracellular matrix deposition & remodeling

Seladelpar (PPARδ) Pharmacology

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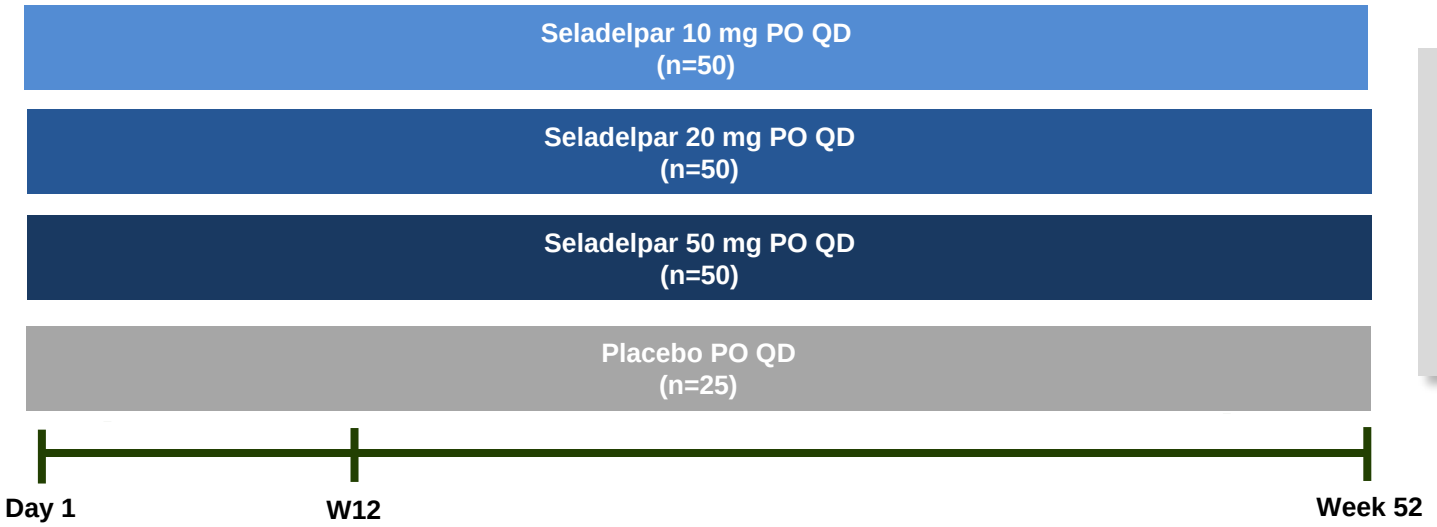
Seladelpar Phase 2b Study in NASH
Paired-liver biopsy 52- week study design

Study design meets FDA/EMA guidance criteria to enable a Ph 3 program



Secondary Outcome: Change in Histology at 52 weeks

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Seladelpar Phase 2b Study in NASH
Enrolled patients reflective of phase 3 population

Population

- Histologically confirmed NASH at baseline
- Liver fat content (LFC) ≥10% by MRI-PDFF
- F1 to F3, NAS ≥ 4; 1 point in each component
- Includes diabetics and non-diabetics

12-Week Outcome Measures

- 12-week relative change in LFC
- Liver biochemistry: ALT, AST, GGT, AP
- Lipid markers: LDL-C, triglycerides
- Other inflammatory markers: hs-CRP

Other Key Outcome Measures

- Safety and tolerability
- 52-week histological improvement in NAS and fibrosis
- LFC and cT1 by LMS
- Liver stiffness by MRE and Fibroscan
- Biochemical fibrosis markers and Histoindex® quantitative digital pathology

Study blinded and ongoing to 52 weeks

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Seladelpar Phase 2b Study in NASH

Baseline demographics and patient characteristics (mITT)

Parameter (Mean ± SD)	Placebo (n = 26)	10 mg (n = 50)	20 mg (n = 47)	50 mg (n = 48)
Age (Years)	54 (10.5)	53 (12.6)	57 (12.0)	53 (11.3)
Male/Female (%)	30.8/69.2	30.0/70.0	31.9/68.1	33.3/66.7
Body Weight (kg)	104.4 (19.9)	95.3 (21.6)	100.7 (22.9)	99.9 (19.9)
MRI-PDFF (%)	22.3 (9.5)	22.0 (7.8)	20.8 (6.1)	20.5 (6.8)
ALT (U/L)	61.0 (34.7)	60.4 (29.6)	57.4 (26.3)	67.6 (40.2)
AST (U/L)	43.5 (24.5)	45.2 (24.9)	46.0 (21.1)	46.3(27.9)
GGT (U/L)	99.3 (177.5)	84.7 (124.4)	97.4 (80.6)	66.5 (45.2)
AP (U/L)	82.1 (34.1)	83.9 (25.1)	81.1 (28.0)	76.5 (21.6)
NAS	5.3 (1.1)	5.2 (1.0)	5.1 (1.0)	5.1 (1.0)
Fibrosis Stage	2.1 (0.65)	2.1 (0.70)	2.3 (0.72)	2.1 (0.65)
LDL-C (mg/dL)	114.2 (45.5)	103.8 (33.0)	111.0 (47.6)	106.7 (40.0)
Triglycerides (mg/dL)	151.2 (51.3)	166.4 (79.5)	173.4 (72.8)	154.2 (93.8)

mITT = modified intent-to-treat population

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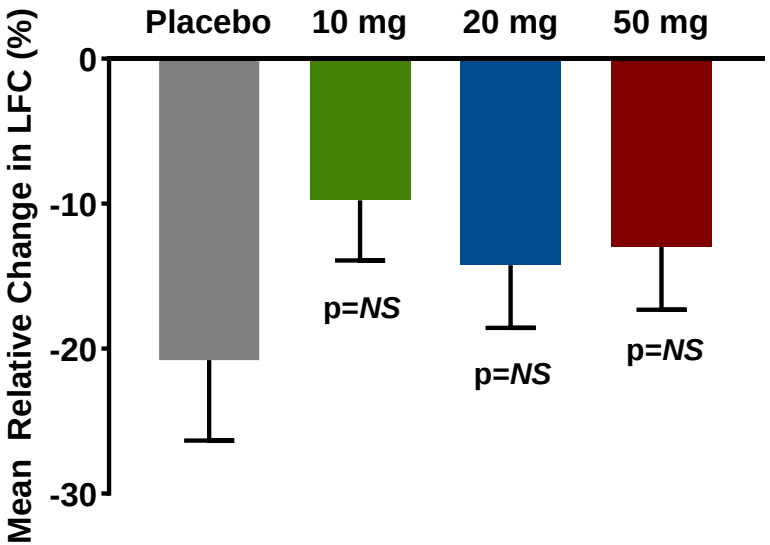
Seladelpar Phase 2b Study in NASH

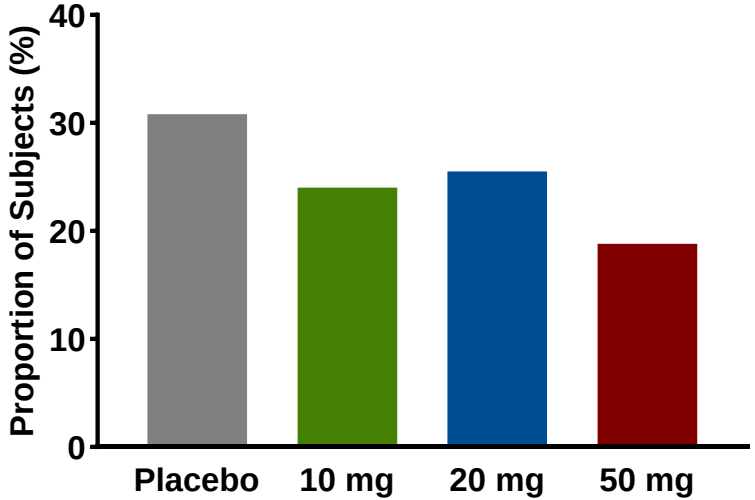
Changes in relative liver fat content by MRI-PDFF at 12 weeks

Comparative Relative Change from Baseline



p-values relative to placebo

Proportion of Subjects with ≥ 30% Relative Change from Baseline



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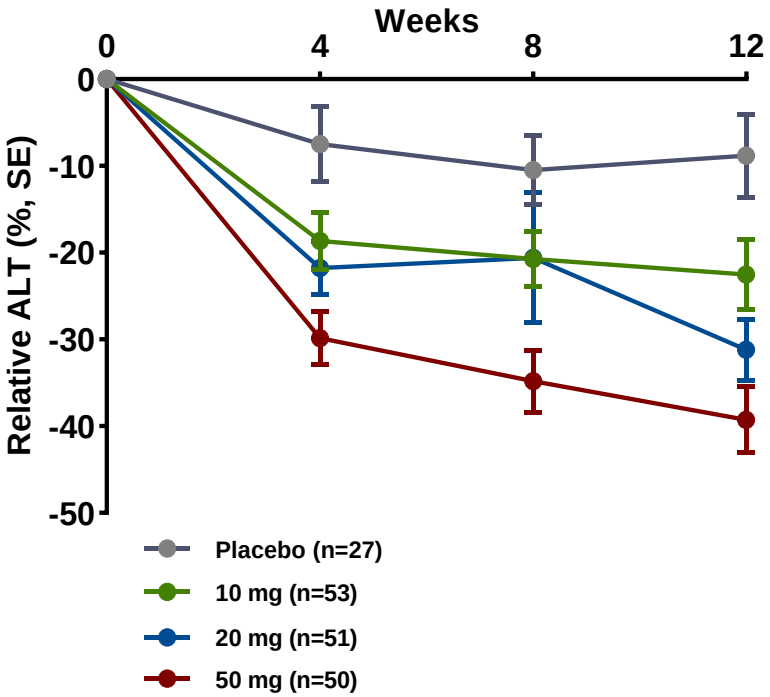
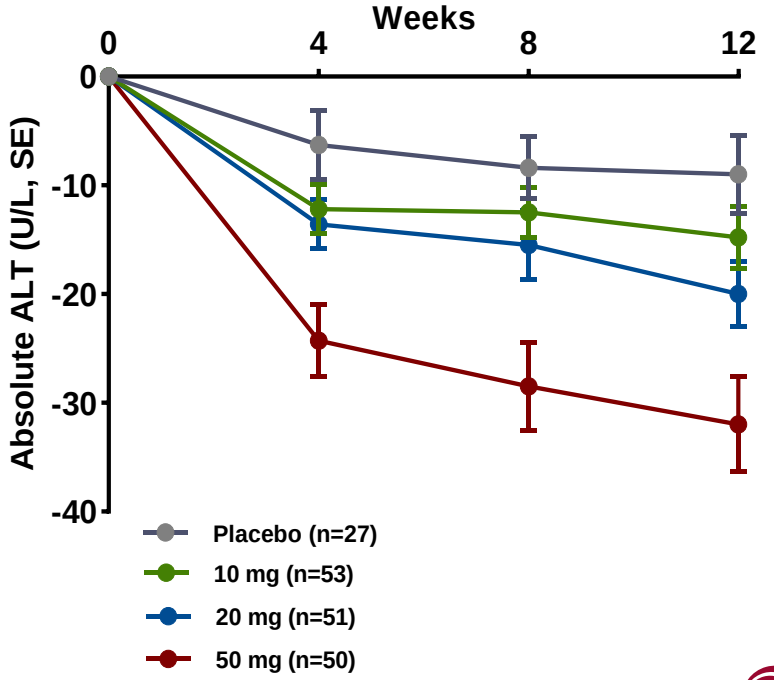
Seladelpar Phase 2b Study in NASH

Positive changes in absolute and relative ALT over 12 weeks

Change in Relative ALT Over Time

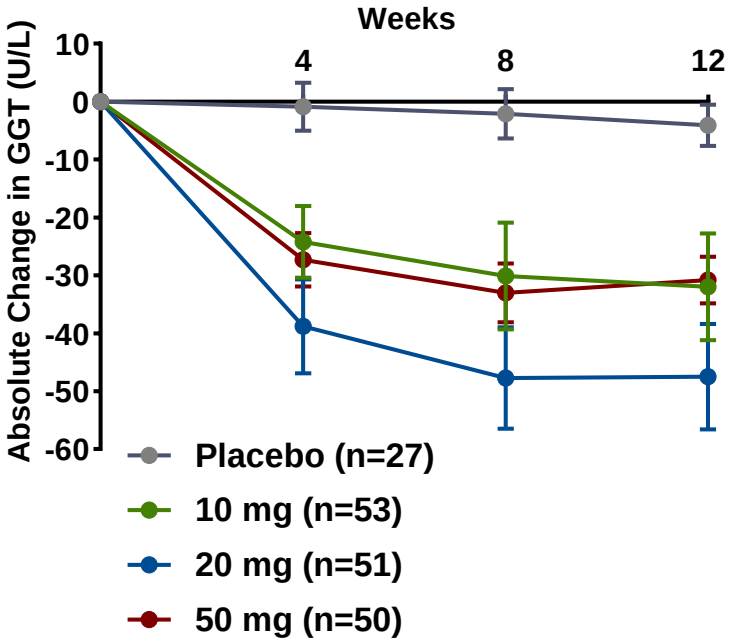


Change in Absolute ALT Over Time

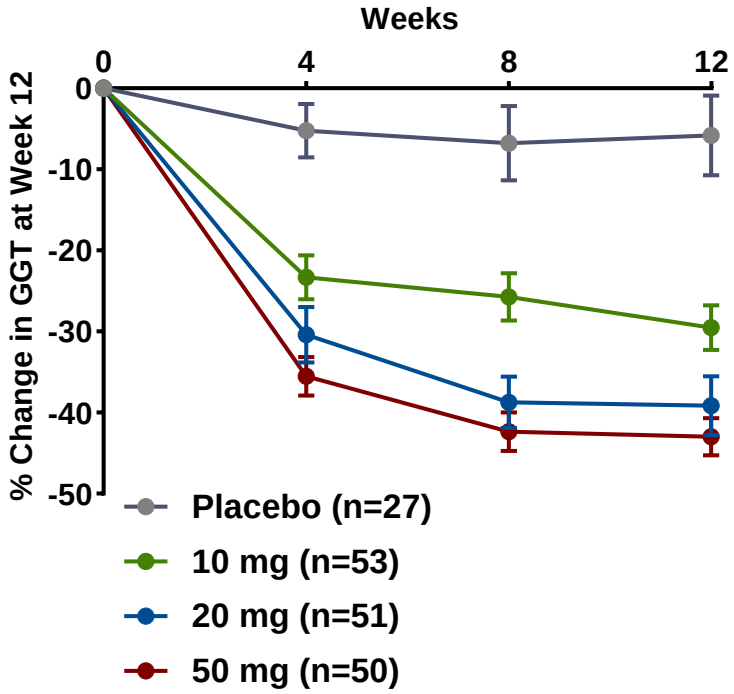


Seladelpar Phase 2b Study in NASH
Positive changes in absolute and relative GGT

Change in Absolute GGT Over Time



Change in Relative GGT Over Time



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Seladelpar Phase 2b Study in NASH

Dose dependent decreases in markers of hepatic injury at 12 weeks

%, LS Mean (SE)	Placebo (n = 27)	10 mg (n = 53)	20 mg (n = 51)	50 mg (n = 50)
ALT	-8.9 (5.1) p=0.08	-22.9 (3.8) p<0.0001	-32.0 (4.0) p<0.0001	-37.5 (4.0) p<0.0001
AST	-12.9 (5.8) p=0.03	-11.6 (4.4) p=0.009	-15.2 (4.5) p=0.001	-17.3 (4.5) p=0.0002
GGT	-4.5 (4.3) p=0.3	-28.2 (3.2) p<0.0001	-37.6 (3.3) p<0.0001	-43.1 (3.4) p<0.0001
AP	4.4 (2.9) p=0.12	-19.1 (2.1) p<0.0001	-25.1 (2.2) p<0.0001	-33.4 (2.2) p<0.0001

ALT, AST, GGT and AP data from safety population; p-values relative to baseline

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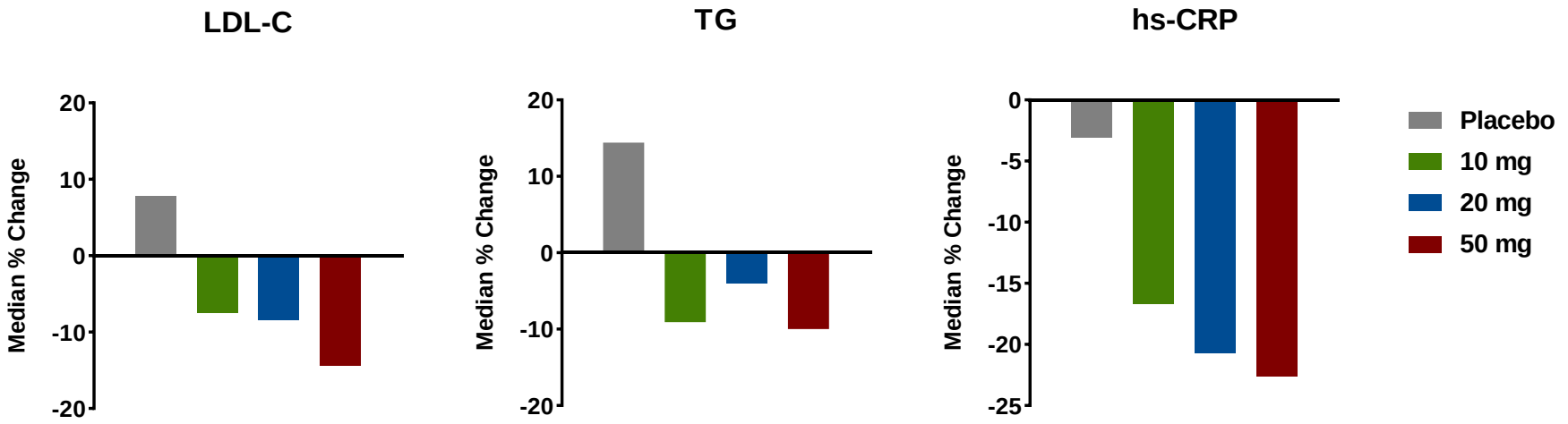
Seladelpar Phase 2b Study in NASH

Positive changes in lipid and inflammation parameters at 12 weeks



LDL-C, TG and hs-CRP data from safety population

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Seladelpar Phase 2b Study in NASH
Additional Pharmacodynamic Measures at Week 12 Interim Analysis

- Dose-dependent decreases of plasma 7α-Hydroxy-4-cholesten-3-one (C4)
  - Inhibition of hepatocellular bile acid synthesis
- Dose-dependent increases in carnitine and short-chain acyl-carnitines
  - Marker of increased lipid metabolism
- No significant effects using the Enhanced Liver Fibrosis (ELF) panel
  - Plasma based biomarkers of fibrosis (use is exploratory in NASH)
- No significant effects were observed in corrected-T1
  - An exploratory MRI method for inflammation associated with NASH
- The study remains blinded until the 52-week liver histology expected in 2Q 2020

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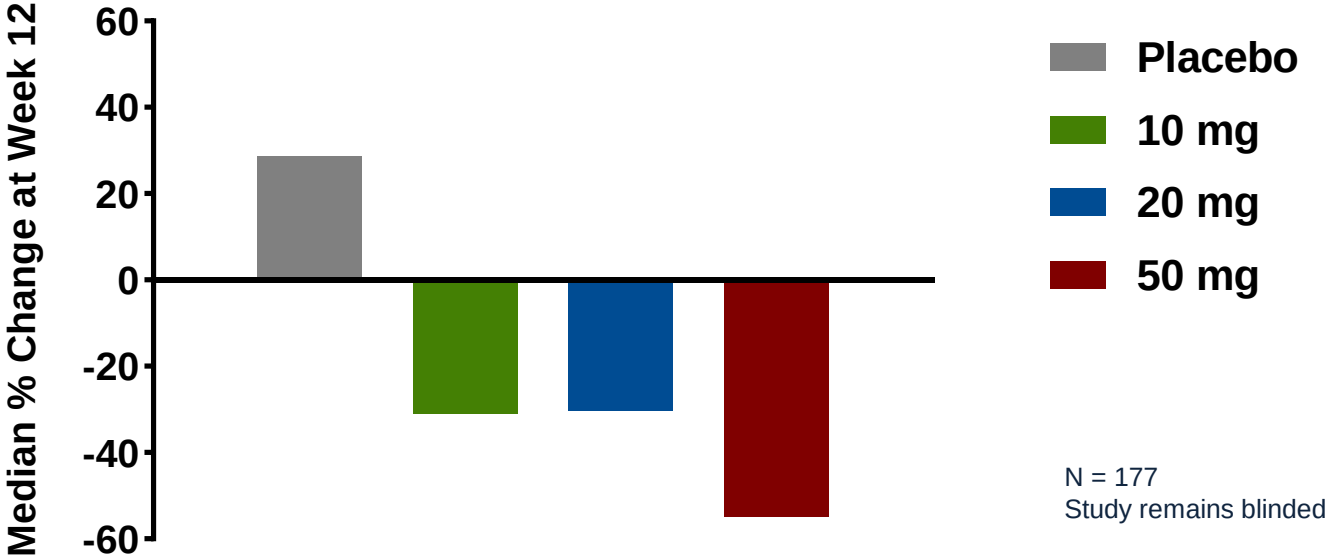
Seladelpar Phase 2b NASH Study
Relative Change in C4 from Baseline to Week 12



Inhibition of hepatocellular bile acid synthesis

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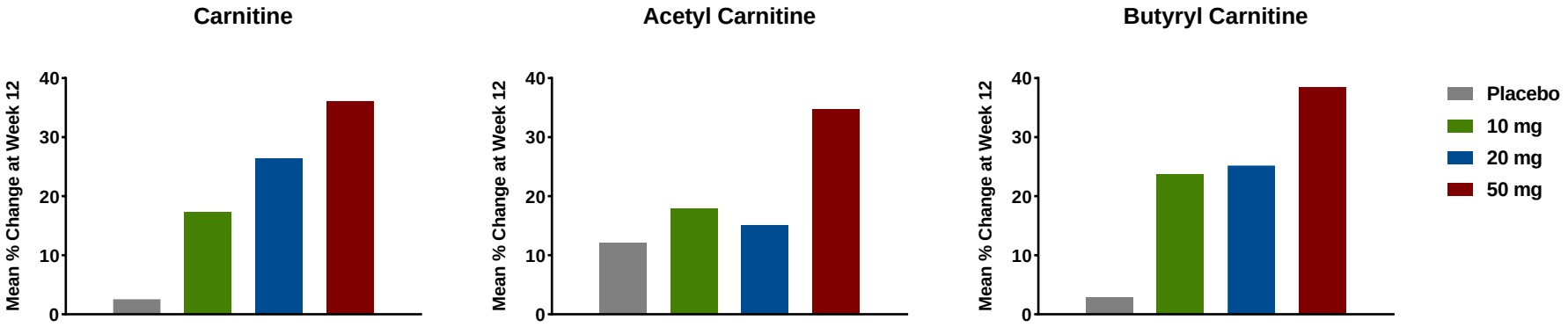
Seladelar Phase 2b NASH Study
Relative Changes in Plasma Acyl-Carnitines After 12 Weeks



N = 177
Study remains blinded

Markers of increased lipid catabolism

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Seladelpar Phase 2b Study in NASH
Safety summary

- Majority of treatment emergent adverse events were mild to moderate and deemed unrelated to study drug
- The most common (>5%) treatment emergent adverse events included nausea, constipation, dizziness, headache, gastroesophageal reflux disease and upper abdominal pain
- Two SAEs both deemed unrelated to study drug
- No Grade 3 or greater ALT/AST elevations

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CymaBay Accomplishments and Goals

2019

- ✓ Breakthrough Therapy Designation
- ✓ 12-week Ph 2b NASH data
- ▪ Initiate Ph 2 PSC study – Q3
- ▪ Complete enrollment of ENHANCE – Q4

2020

- ▪ Ph 2 PBC full data – Q1
- ▪ 52-week Ph 2b NASH data (histology) – Q2
- ▪ Complete 52-week treatment period of ENHANCE – H2

2021

- ▪ ENHANCE data – H1
- ▪ PSC Ph2 data – H2
- ▪ NDA filing PBC – H2

Improving the lives of patients with liver diseases

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