

# Corporate Presentation

January 2024

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# Corporate Highlights

## COMMITTED TO TRANSFORMING THE LIVES OF PATIENTS

Focused on addressing significant unmet needs, and improving patients' lives

## SETTING A NEW BAR IN PBC WITH SELADELPAR

Redefining treatment with the first delpar, an investigational agent for the treatment of PBC, to improve biochemical normalization & alleviate symptoms

## INDUSTRY LEADING TEAM TO DELIVER FIRST LAUNCH IN PBC

Years of drug development, commercial launch, and corporate finance experience to transform PBC care by bringing seladelpar to patients

## BUILDING ON SELADELPAR SUCCESS TO ADVANCE DEVELOPMENT

Deep clinical and scientific expertise to transform treatment of metabolic, inflammatory and fibrotic diseases

# CymaBay is committed to improving the lives of people with liver and other chronic diseases

## Mission

Guided by a **deep commitment to patients**, CymaBay **transforms the lives** of people suffering with chronic liver, digestive tract, or inflammatory diseases, by **developing innovative medicines** that restore health and improve life

## Vision

Our vision is to **conquer metabolic, inflammatory and fibrotic diseases**, so that patients can lead **fulfilling lives without suffering**



# Our leadership team has years of experience to successfully transition from a clinical to commercial-stage company



**Sujal Shah**  
President & CEO



**Charles McWherter**  
CSO & President of R&D



**Harish Shantharam**  
Chief Financial Officer



**Klara Dickinson**  
Chief Regulatory Officer



**Paul Quinlan**  
General Counsel



**Patrick O'Mara**  
SVP Business Development






**Becki Filice**  
SVP Portfolio & Product

   
A Member of the Roche Group



**Ben Kozub**  
Head of Commercial



**Robert Martin**  
SVP Manufacturing





**Ken Boehm**  
SVP Human Resources

# CymaBay is moving forward with tremendous momentum in anticipation of our first-product launch and beyond

## Build

up to  
2023

- Multiple **dose-ranging** safety and efficacy studies in **PBC** (2015-2020)
- **ASSURE** long-term study initiated (2021)
- Seladelpar **licensed to Kaken for Japan**
- Pivotal study, **RESPONSE, achieves statistical significance\***
- **Medical affairs** buildout and deployment
- Initiation of **IDEAL** study (2023)
- **AFFIRM** outcomes study initiated (2023)
- **US NDA submitted** (2023)

## Execute

2024

- Commercial & Medical launch readiness preparation
- **US NDA approval**
- **UK and EU MAA review**
- **US Launch in PBC<sup>^</sup>**

## Expand

2025+

- UK & EU Approval
- **IDEAL results** in broader PBC population
- Potential to **benefit larger patient population** beyond original launch
- Japan launch by partner

\*Statistical significance on primary and key secondary endpoints

<sup>^</sup>Based on FDA granting a priority review

# Primary Biliary Cholangitis (PBC) is a rare, chronic and progressive liver disease

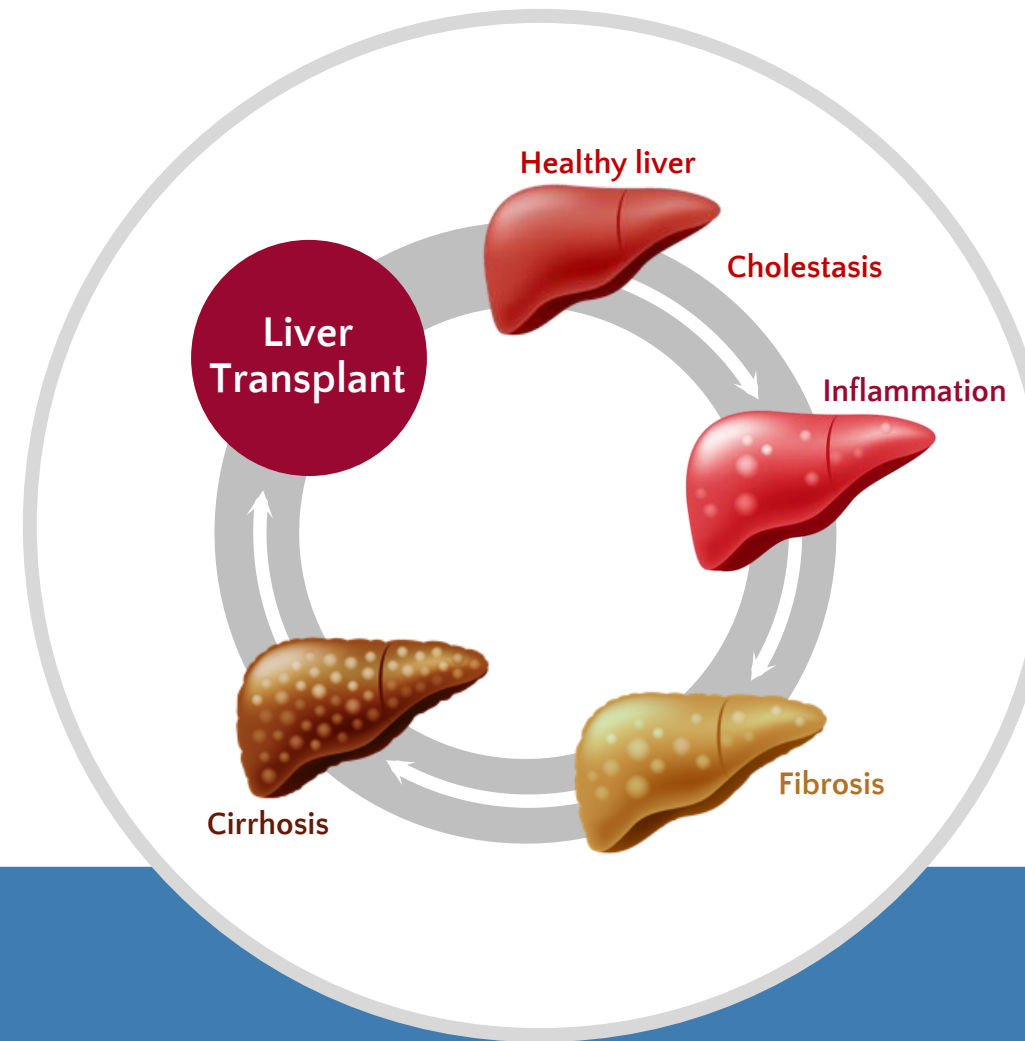
Autoimmune liver disorder leading to **progressive liver damage and failure**

Affects 1 in 1,000 women over 40; **~130k US patients**  
Of these, **~85k are diagnosed**, and **~70-75k treated**

**Significant symptom burden**, including pruritus and fatigue, which **impacts patient QoL**

Treatment goals are to **slow disease progression** and **reduce symptom burden**

**Attaining alkaline phosphatase (ALP)  $\leq 1x$  upper limit of normal (ULN) or bilirubin levels  $\leq 0.6 \times$  ULN in observational studies was associated with the lowest risk for liver transplant or death in patients with PBC**



# Currently available PBC treatments do not adequately improve patient response and symptom burden

~60%

of patients **do not normalize ALP** on 1L UDCA treatment



patients without normalized ALP are at **increased risk of progression, transplant and death**

up to 40%

of patients **progress to cirrhosis** over the course of the disease



**Limited 2L treatments** for patients who have or progress to cirrhosis

up to 40%

experience **moderate-to-severe pruritus**, reducing quality of life



**No effective anti-pruritic options**, with potential worsening of itch with Ocaliva

***Safe and effective treatments to normalize ALP and relieve PBC symptoms across the spectrum of disease are needed to improve patient outcomes***



# Primary Biliary Cholangitis

**Seladelpar, an investigational agent, has potential to meet the needs of PBC patients with better efficacy and tolerability than current 2nd line therapy**

**Orphan (FDA, EMA), Breakthrough Therapy (FDA) and Priority Medicine (EMA) designations**



# Seladelpar is the first, potent and selective PPAR delta agonist – or delpar – being developed for the treatment of PBC

## DECREASE BILE ACIDS

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

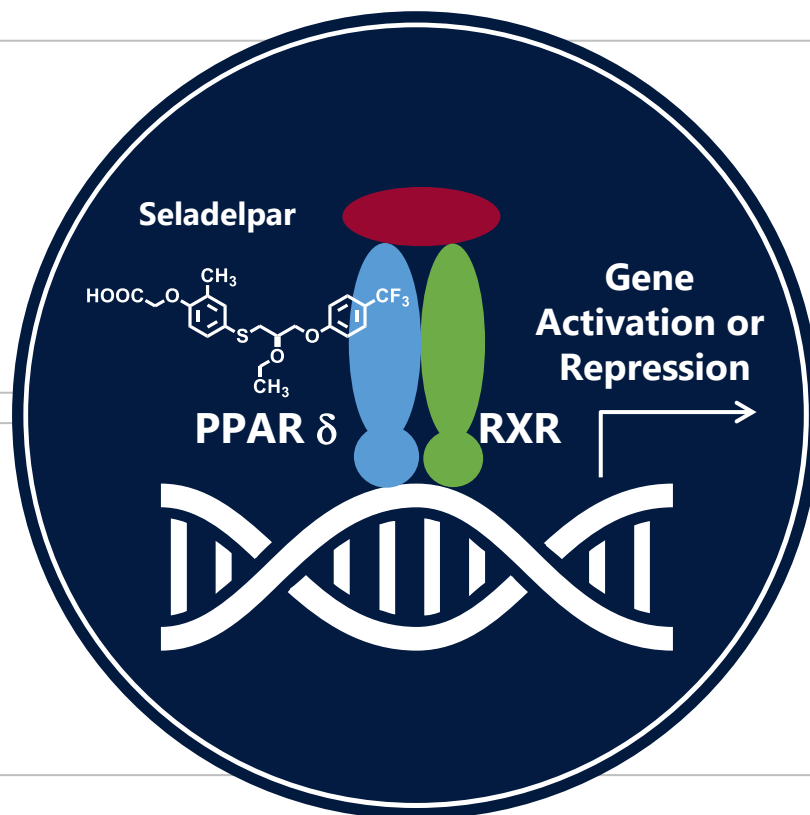
HEPATOCYTE

CHOLANGIOCYTE

## ANTI-PRURITIC

- ↓ Serum IL-31
- ↓ Bile acids

HEPATOCYTE



## ANTI-INFLAMMATORY

- ↓ NF $\kappa$ B-dependent gene activation
- ↓ Inflammatory cytokines
- ↓ hs-C-Reactive Protein

KUPFFER CELL

MACROPHAGE

## INCREASE LIPID METABOLISM

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

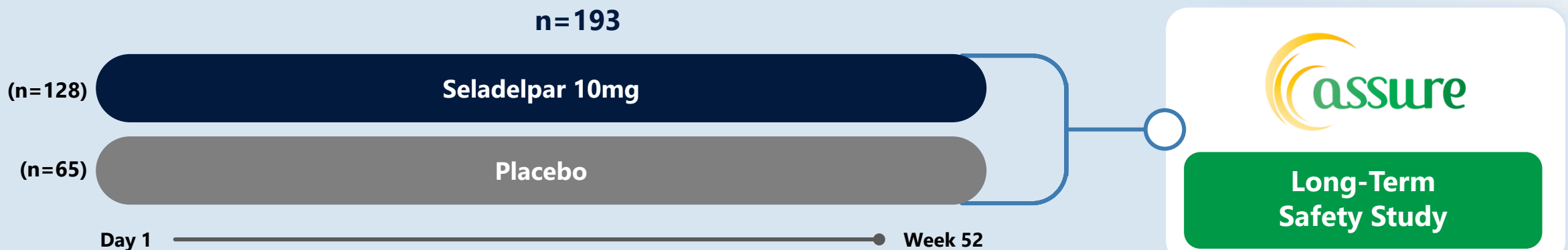
HEPATOCYTE

Seladelpar targets multiple cell types important in liver disease

# Phase 3 study of seladelpar in patients with PBC

*Placebo-controlled, double-blind 52-week pivotal study*

Patients with PBC and an inadequate response or an intolerance to ursodeoxycholic acid (UDCA)



## Primary Outcome:

- Composite responder rate: **1)** ALP  $< 1.67 \times \text{ULN}$ , **2)**  $\geq 15\%$  decrease in ALP, **3)** total bilirubin  $\leq \text{ULN}$

## Secondary Outcomes:

- Proportion of patients with ALP  $\leq 1.0 \times \text{ULN}$  at 12 months
- Change at 6 months in pruritus in subjects with baseline Numerical Rating Scale  $\geq 4$  using daily e-diary

# RESPONSE enrolled a high-risk PBC patient population

## Demographics & Baseline Characteristics

Placebo  
(n=65)

Seladelpar 10mg  
(n=128)

Female, n (%)

60 (92.3)

123 (96.1)

Age, years

57.0 (9.17)

56.6 (9.99)

**Pruritus NRS  $\geq 4$**

**23 (35.4)**

**49 (38.3)**

UDCA Intolerant, n (%)

3 (4.6)

8 (6.3)

**ALP**

**ULN: 116 U/L**

**313.8 (117.68)**

**314.6 (122.96)**

**Total bilirubin**

**ULN: 1.1 mg/dL**

**0.74 (0.31)**

**0.77 (0.31)**

# RESPONSE results suggest seladelpar may optimize treatment for some PBC patients who have not responded to UDCA

## Key RESPONSE Results

**62%**

achieved primary composite endpoint for **biochemical response**

**25%**

**normalized ALP** by 12 months

**3.2pt**

**average reduction in NRS scores** in patients with moderate-to-severe pruritus

**0**

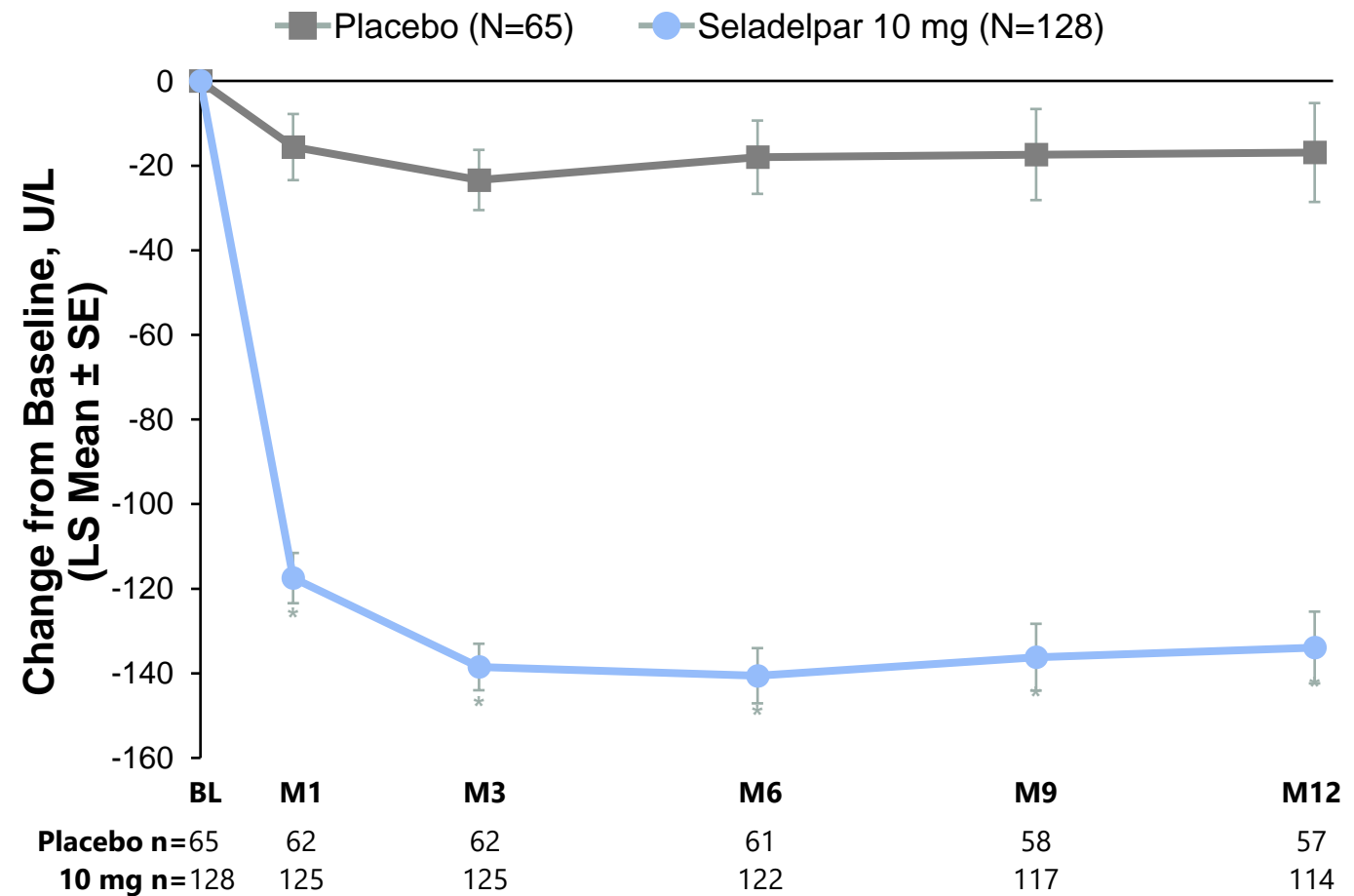
**Treatment-related serious adverse events** in the study

### Seladelpar may help optimize patient treatment by:

- High rates of composite response and **ALP normalization**
- Statistically significant **improvement in pruritus**
- **Safety and tolerability profiles comparable** between treatment and placebo arms

# Seladelpar significantly reduced ALP

## ALP Change from Baseline (12 months)



134  
U/L

reduction in ALP  
at 12 months,  
~8x greater than placebo

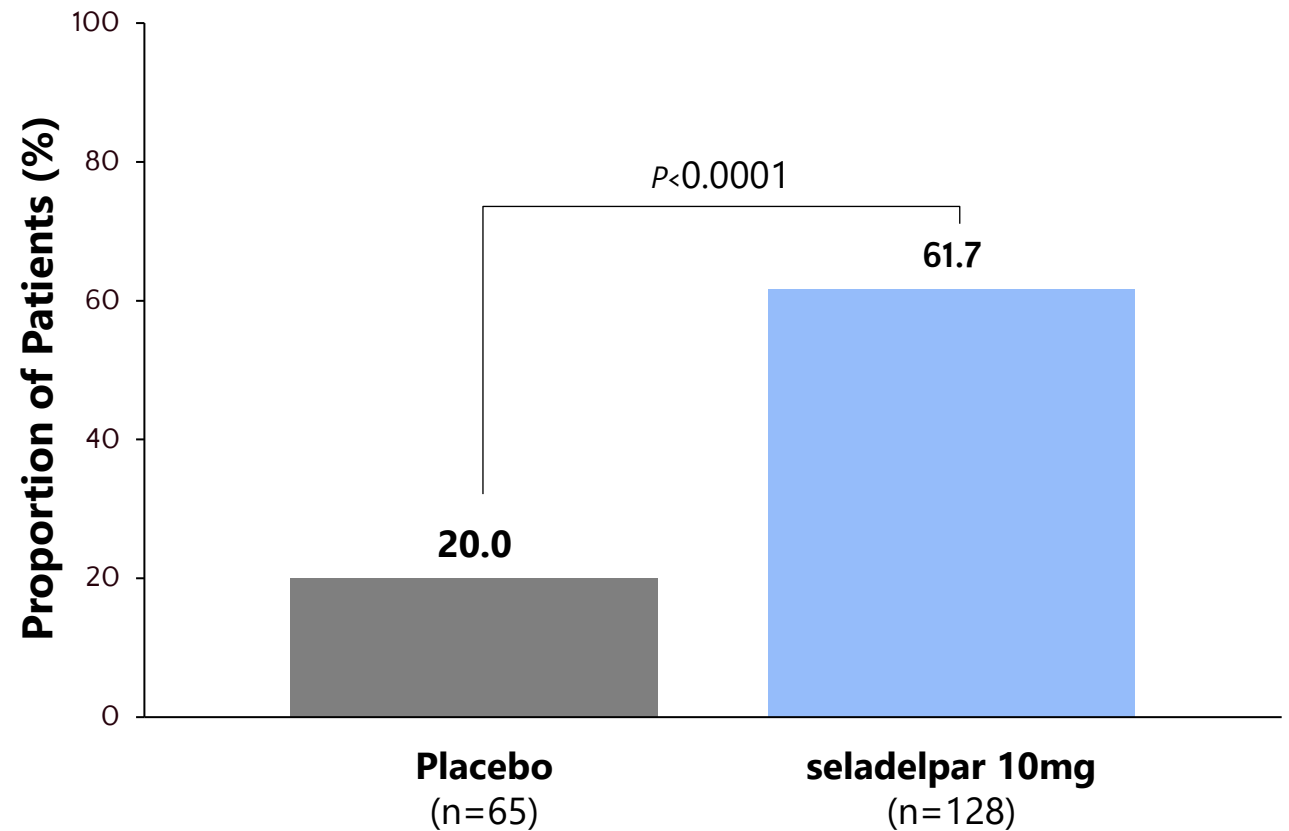
U/L change from Baseline

P\*P < 0.0001 vs placebo. Note: ITT analysis set. Abbreviations: ALP=alkaline phosphatase, BL=baseline, ITT=intent-to-treat, LS=least squares, M=month, SE=standard error.  
Source: Table 14.2.8.4.

# Seladelpar demonstrated high rates of biochemical response at 12 months

## Primary Composite Biochemical Endpoint

ALP < 1.67x ULN,  $\geq 15\%$  decrease in ALP, TB  $\leq$  ULN



62%

of seladelpar patients achieved the primary composite endpoint

ALP < 1.67x ULN,  
 $\geq 15\%$  decrease in ALP, TB  $\leq$  ULN

# Seladelpar effects on ALP normalization supports a new PBC treatment goal

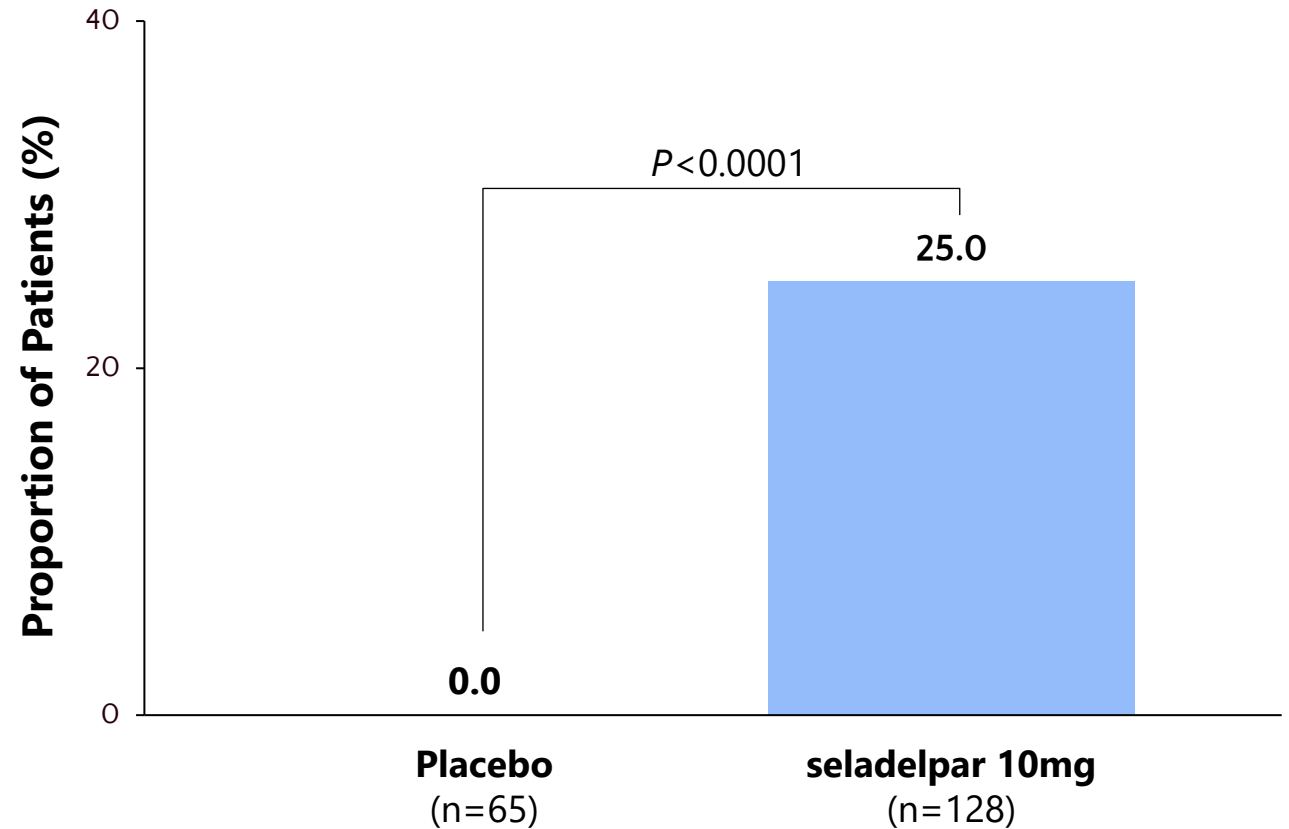
25%

of seladelpar patients  
normalized ALP  
by 12 months

ALP <1x ULN

## Secondary Endpoint of ALP Normalization

ALP <1x ULN



P value by CMH test  
Source: Table 14.2.3.1



# Seladelpar is the only treatment in Phase 3 that reduced\* pruritus in PBC

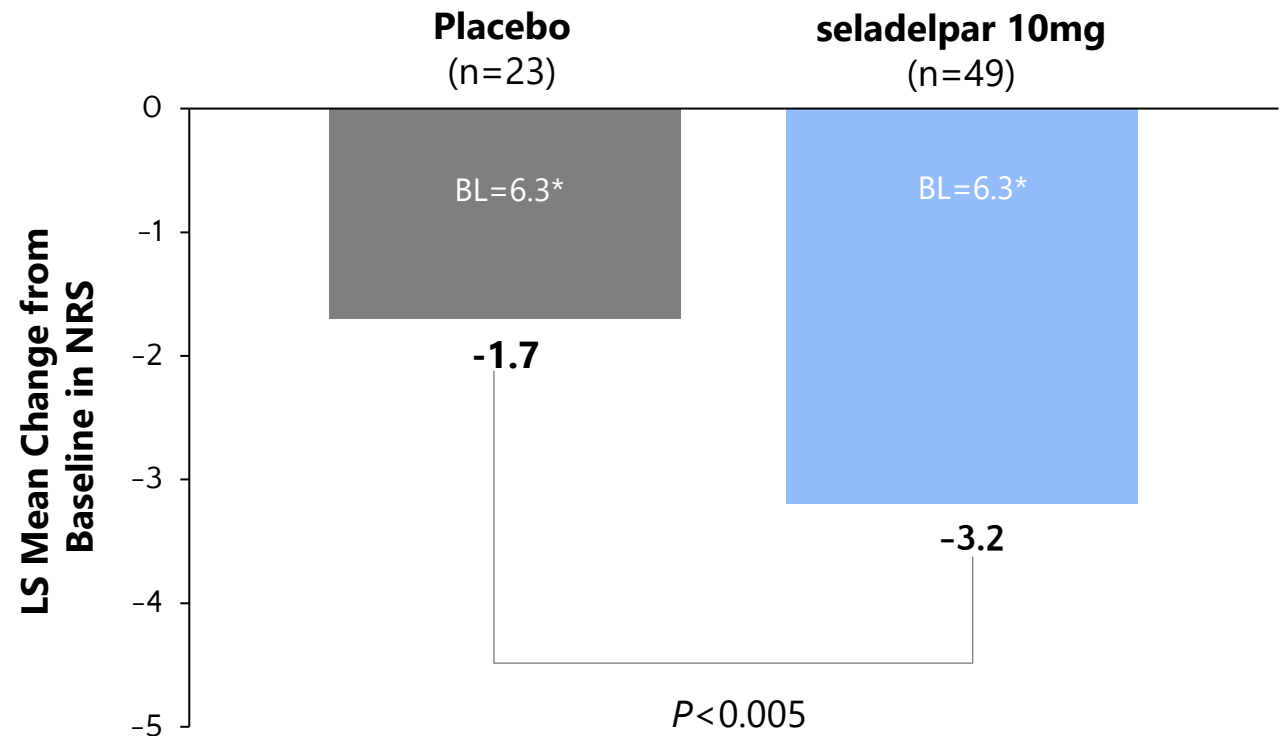
## Secondary Endpoint of Change at 6 Months in Pruritus

Among patients with baseline Moderate-Severe Pruritus (NRS  $\geq 4^{**}$ )

3.2  
points

average reduction in NRS scores with seladelpar for moderate-to-severe pruritus patients

LS Mean Change in NRS



\* Statistically significant reduction; \*\*The mean baseline NRS was 6.3 for all patients having a baseline NRS  $\geq 4$

LS Mean and P values by MMRM model

Source: Table 14.2.5.1

# Seladelpar appeared safe and well tolerated across the **RESPONSE** study population

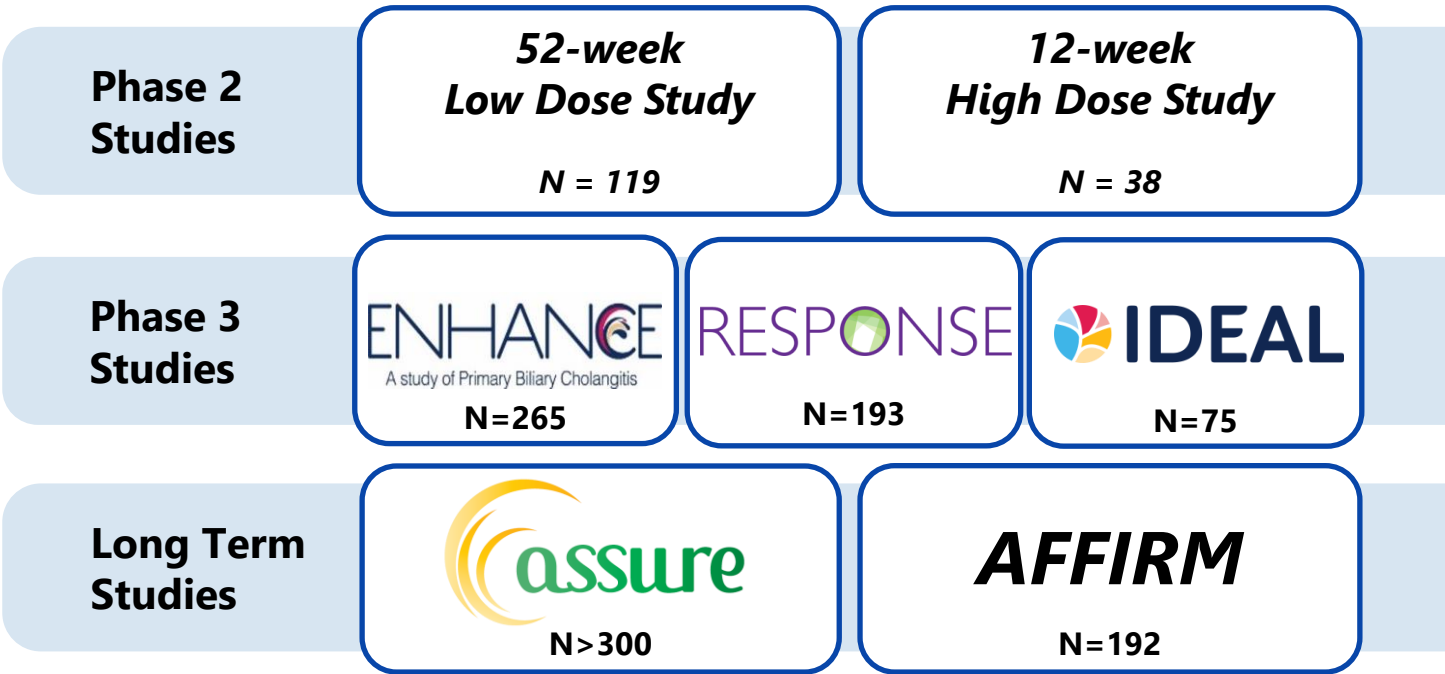
RESPONSE

**Safety was comparable between placebo and seladelpar groups,**  
and consistent with previous studies

Treatment-emergent adverse events, serious adverse events & discontinuations  
were generally **balanced across the treatment and placebo arms**

There were **no treatment-related serious adverse events** in the study

# Seladelpar is supported by a robust clinical program in PBC



**Robust Clinical Program**  
Seven clinical studies across PBC patient spectrum

**Extensive Patient Experience**  
with >500 PBC patient exposures



# The IDEAL study aims to reset PBC treatment goals to ALP normalization

Phase 3 study Intended to Determine the Effects of seladelpar on normalization of Alkaline phosphatase Levels in subjects with PBC

Add-on to UDCA in Patients With ALP  $>1.00$  ULN and  $<1.67 \times$  ULN

(n=50)

Seladelpar 10mg

(n=25)

Placebo

Day 1

Week 52

## PRIMARY ANALYSIS:

- ALP normalization at 52 weeks
- The primary endpoint is ALP  $\leq 1.0 \times$  ULN

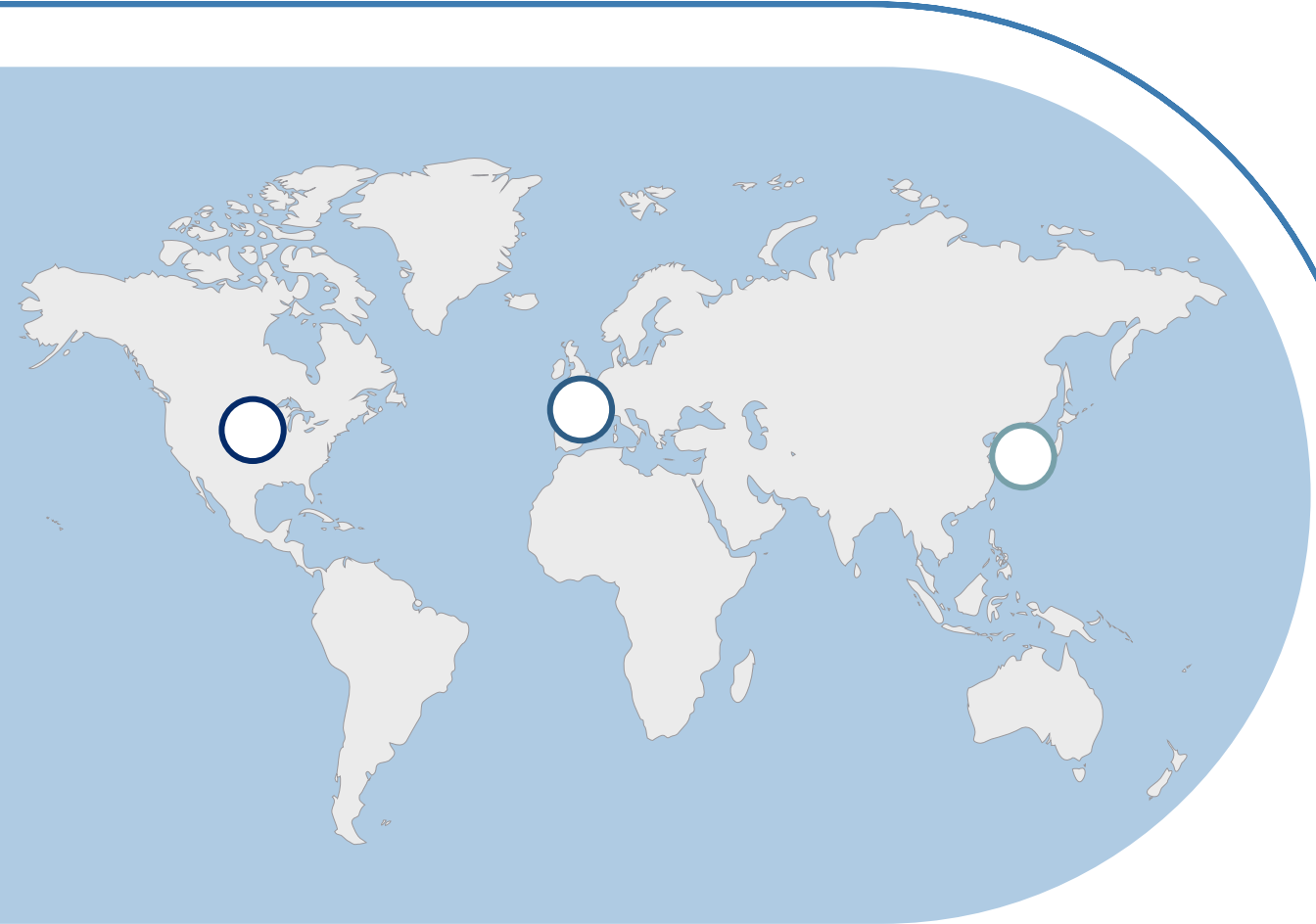
## SECONDARY ANALYSES:

- Improvement in cholestatic pruritus at 6 months
- Safety and tolerability

## Why IDEAL?

- To evaluate potential benefits of seladelpar on **patients who do not meet current guidelines for second-line treatment** and have **not typically been included in clinical research** (ALP 1.00 – 1.67xULN)
- **Activate undertreated patients** by generating data that may **support increased response** for patients in **need of additional treatment**

# There is a significant global opportunity for seladelpar in 2L PBC



### Estimated PBC Patient Volume

**Diagnosed**                      **Total Treated**

**US**

~85k                      ~70-75k

**EU**  
UK & EU4

~100K                      ~93K

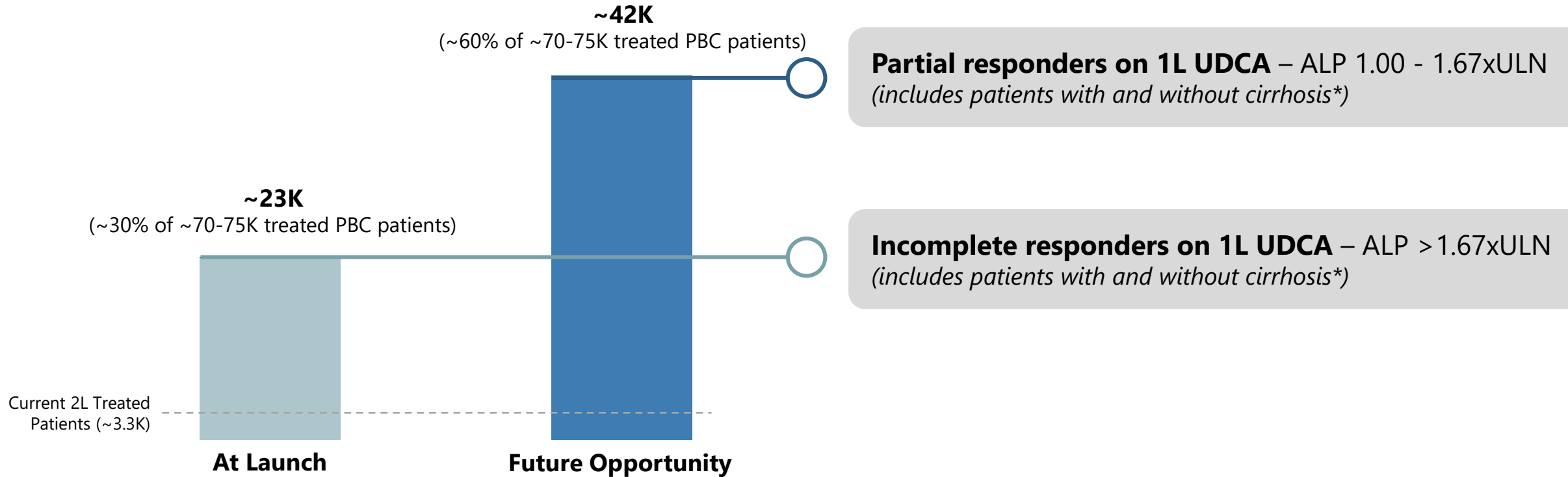
**Asia**  
JP & China

~300 – 415k                      ~285 – 390k

# Seladelpar has opportunity to reset 2L PBC treatment, with potential to address 60% of ~70-75k treated US population

## US Seladelpar 2L Market Opportunity

Across ~70-75K Treated PBC Patients, US



**Significant pruritus improvement will be a strong driver for seladelpar opportunity and treatment choice across all 2L patient segments**

# CymaBay aims to bring seladelpar to every 2L patient living with PBC who may benefit

## Commercial Priorities



### Reset Expectations

- Address **patient needs across the PBC journey**
- Provide **solutions addressing both immediate and long-term treatment goals**



### Drive Rapid Adoption

- Target **PBC high volume treaters**
- Address HCP **treatment drivers and barriers**



### Maximize Patient Access

- Facilitate **rapid and seamless coverage & reimbursement**
- Develop **comprehensive, solution-based patient support services**



### Pursue Launch Excellence

- Establish a **fit-for-purpose commercial model** to drive successful US launch
- **Optimize global patient reach** by leveraging local expertise

# CymaBay will focus on improving treatment success along the continuum of PBC care



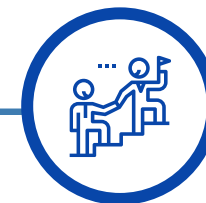
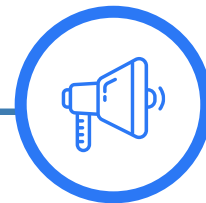
## Diagnosis

## Treatment

## Long-term Management

### Patient Needs

- **Clear information from HCPs** on PBC and its management
- **Recognition** of PBC symptoms
- Details on treatment options to improve **liver biochemistries and debilitating symptoms**
- Guidance to address **day-to-day challenges & long-term success**
- **Effective & affordable treatment** to slow progression & relieve symptoms
- **Support holistic health** while living with PBC



### CymaBay Solutions

- Educate on **PBC expectations**, including symptom management
- **Provide trusted resources** to support Patient–HCP dialogue
- **Support treatment goal setting** with PBC treatment education
- Foster **ongoing, meaningful conversations** on quality of life
- **Cultivate a PBC network** that includes the advocacy community
- Facilitate access to **efficacious, safe & tolerable** treatment options addressing **patients' total health**
- Support HCP & patient focus on **symptom control & treatment compliance**



# Seladelpar can help PBC treaters optimize treatment success for their 2L patients

## CymaBay Approach

### Targeting High Volume PBC Treaters

~**6.7K** HCPs represent ~**80%** of PBC market

~**5K** of these Top PBC Treaters are Gastros & Hepatologists

### Leveraging Practice Demographics & Expertise

- Academic, hospital systems, and community points-of care
- Liver disease centers of excellence & high-volume group practices
- Expertise treating and managing the spectrum of PBC patients

### Addressing HCPs' Treatment Priorities and Gaps

- **Want to control or normalize ALP**, but need more **efficacious options**
- Managing **pruritus is a priority**, but have **limited options to offer** patients
- **Actively monitor disease progression**, but **may delay 2L treatment** due to lack of effective & tolerable options

## Seladelpar may enable physicians to

### Treat to **NORMAL**

*Provide 2L treatment option that can significantly lower ALP*

### Treat **SYMPTOMS**

*Address total health of patient – both liver health & pruritus*

### Treat **EARLY**

*Optimize treatment by initiating effective & tolerable 2L therapy*

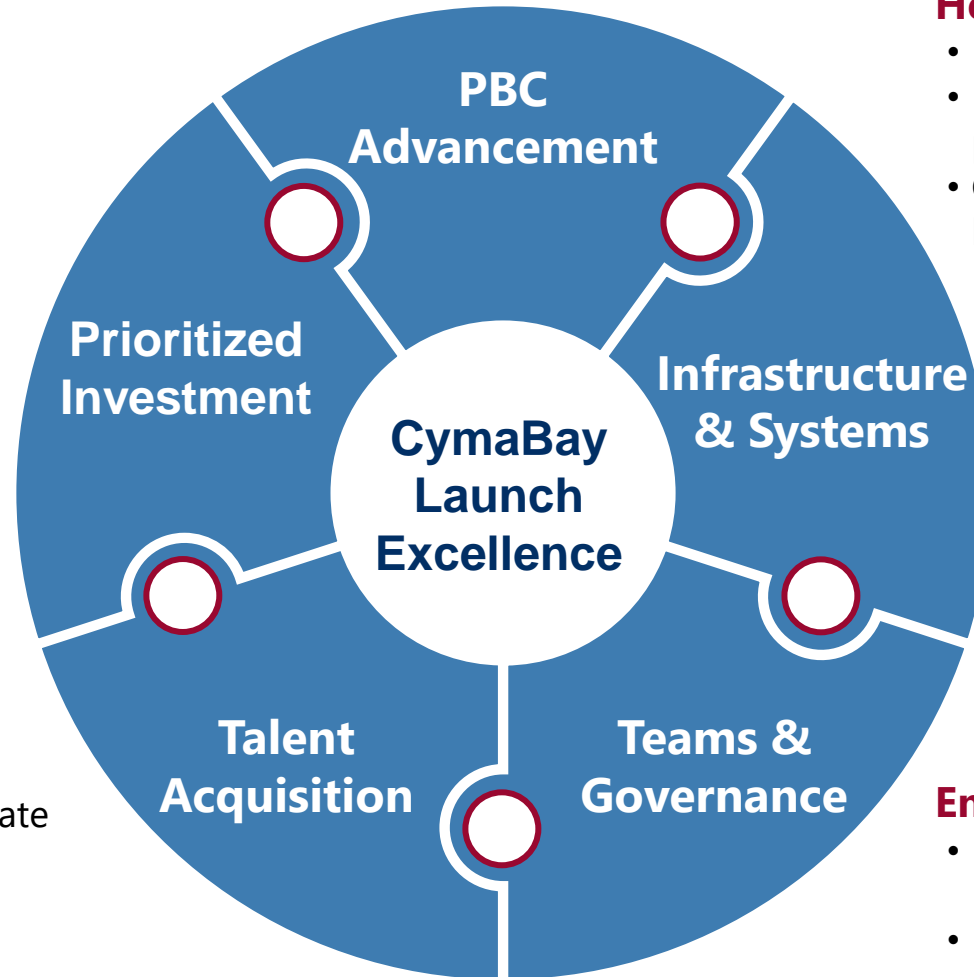
# The commercial organization is focused on our patients, people, and priorities to fuel our first product launch

## Align investments with strategy

- Identify, develop & execute launch critical initiatives
- Gate investment decisions to key milestones
- Invest in life-cycle management to address existing unmet needs

## Hire best talent to drive success

- Hire for critical roles at the right time
- Onboard employees to support immediate contribution & future retention



## Help lead a new paradigm in 2L PBC

- Redefine care for people living with PBC
- Ensure seladelpar is recognized as the optimal patient solution
- Collaborate alongside PBC advocacy and healthcare communities to maximize impact

## Fit-for-purpose operating model

- Create internal capabilities to enable first and future product launches
- Leverage technology to enable agile decision-making and maximize productivity and impact

## Emphasize cross-functional collaboration

- Ensure cohesive decision-making and management decisions
- Streamline processes to support compliant cross-functional collaboration

# CymaBay will offer access solutions so patients can start and stay on seladelpar once approved

## Current Patient Access Situation

- For patients and their HCPs, **2L treatment** often is **perceived as difficult to access**
- **Persistency with OCA 2L treatment is lower overall** than initial treatment with UDCA
- Supplementary **support services needed** beyond financial assistance
- **2L treatment has additional requirements** in most cases
  - prior authorization, step edits or CMS medical exception

**Patient access & affordability needs require more focus and attention**

## CymaBay Solutions

### Leverage differentiated seladelpar value proposition vs. standard of care (SoC)

- ▲ High rates of biochemical normalization
- ▲ Tolerable treatment
- ▲ Reduction in pruritus
- ▲ Positive impact on QoL

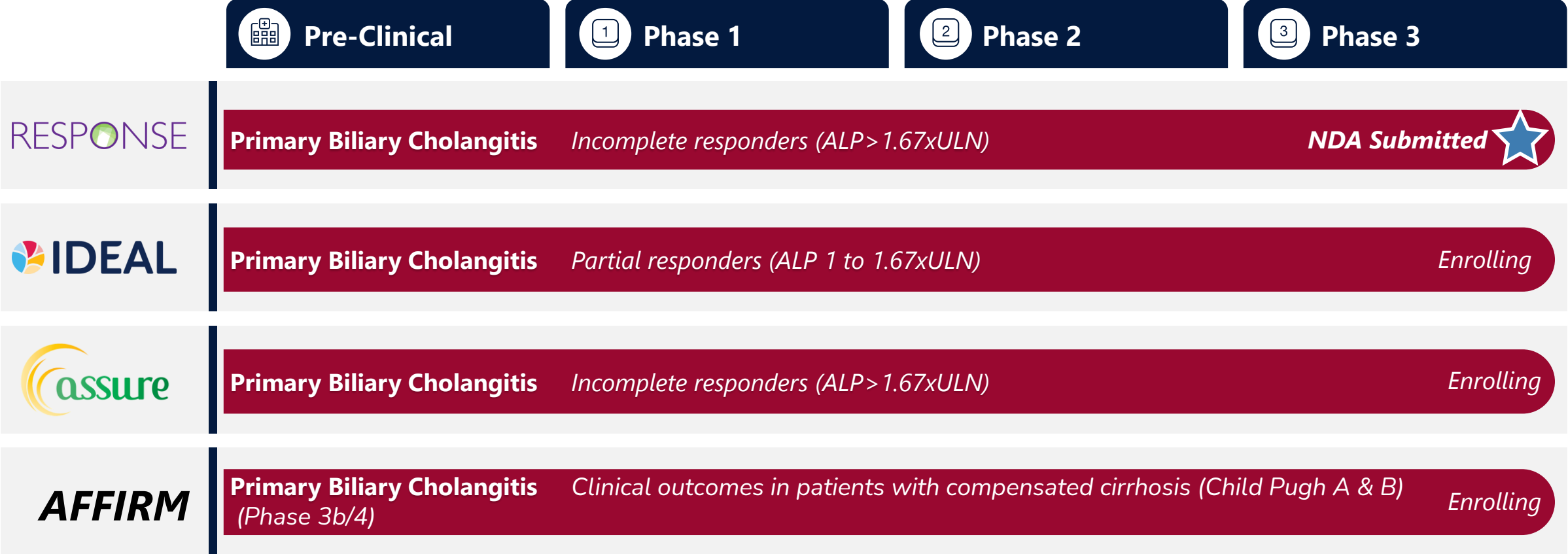
### Provide specialized rare disease patient services

- Comprehensive HUB services designed for PBC patient need
- Benefits investigation, qualified financial assistance, and patient resources
- Offer initial and ongoing counseling, especially adherence/compliance

### Support payer policies for seladelpar

- Pre-approval information exchange, including PBC disease burden education
- P&T committee preparation via AMCP dossier
- National/region account support to top commercial & Medicare plans

# Seladelpar\* may serve as a foundational second-line treatment for PBC



**CymaBay will continue to leverage its expertise in fibrotic, inflammatory and metabolic diseases to develop therapeutics for rare, high unmet need indications**

28 \*Seladelpar is an investigational drug with breakthrough designation. Seladelpar has not been approved for use in any indication by the FDA, EMA, or other regulatory agencies. Phase 3 clinical trials for seladelpar in PBC are ongoing.



Thank You