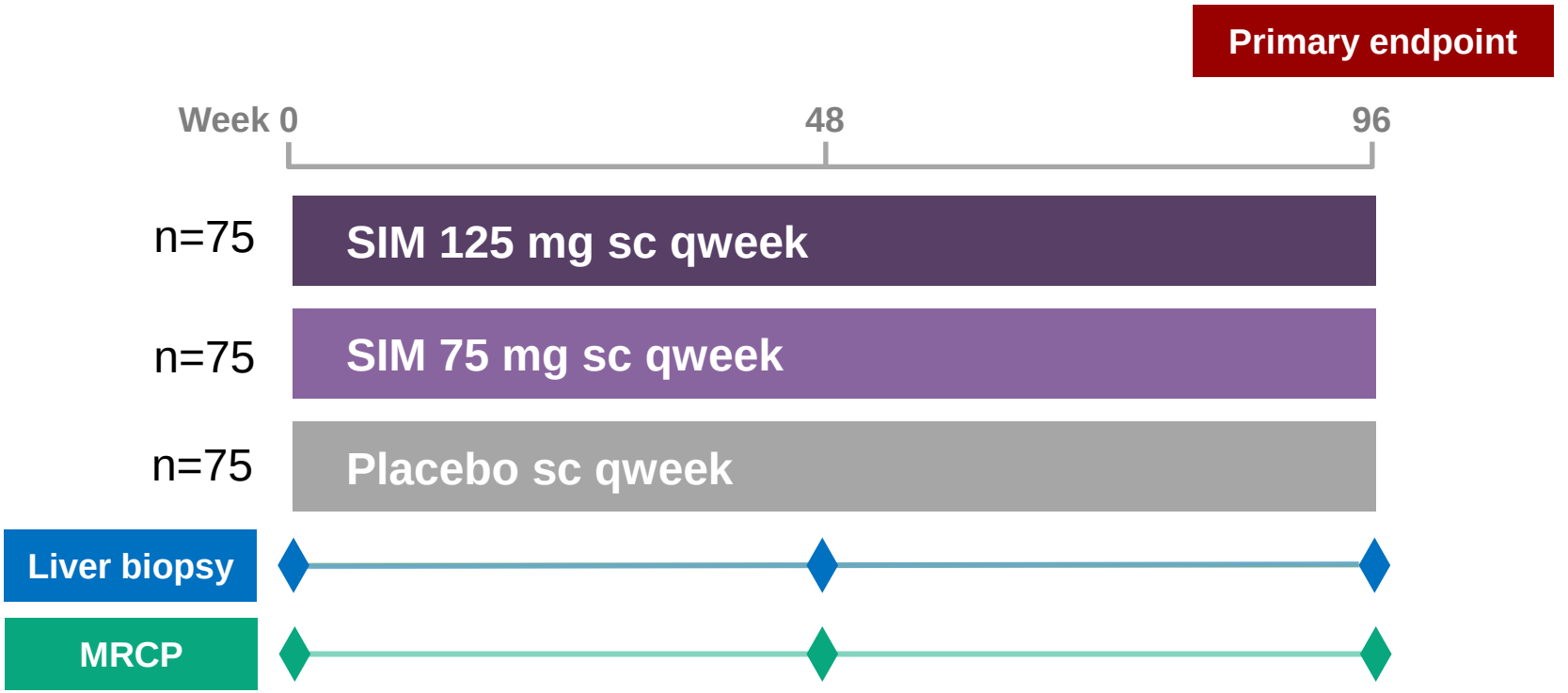
Patient Recruitment and Retention in Phase 2 PSC Studies

Rob Myers, MD
Vice President, Liver Diseases
Gilead Sciences, Inc.

PSC Forum
EASL 2018, Paris, France
April 10, 2018

Simtuzumab (SIM) for PSC: Phase 2 Study Design



Purpose: To determine the safety, tolerability, and efficacy of SIM in patients with PSC.

Population: Compensated PSC (biopsy and MRCP)
Inactive IBD

Muir AJ, et al. EASL 2017.

SIM for PSC: Inclusion/Exclusion Criteria

Major Inclusion Criteria

- 18-65 years
- Chronic cholestasis >6 months
- PSC on MRCP during screening
- Liver biopsy consistent with PSC during screening
- No other liver diseases
- AST/ALT <10 x ULN
- Creatinine <2 mg/dL

Major Exclusion Criteria

- History of decompensation
- Other liver diseases
  - AMA+, HCV RNA+, HBsAg+, alcohol
- Active IBD
  - Original: partial Mayo >2, any steroids or TNF
  - Amendment: partial Mayo >4, bleeding score >1, any steroids, TNF, or $\alpha 4\beta 7$
- Cholangiocarcinoma
  - If dominant stricture, cholangiocarcinoma ruled out (investigator discretion)
- Ascending cholangitis within 60 days
- Percutaneous drain or stent
- Open wound or major procedure within 30 days

Muir AJ, et al. EASL 2017.

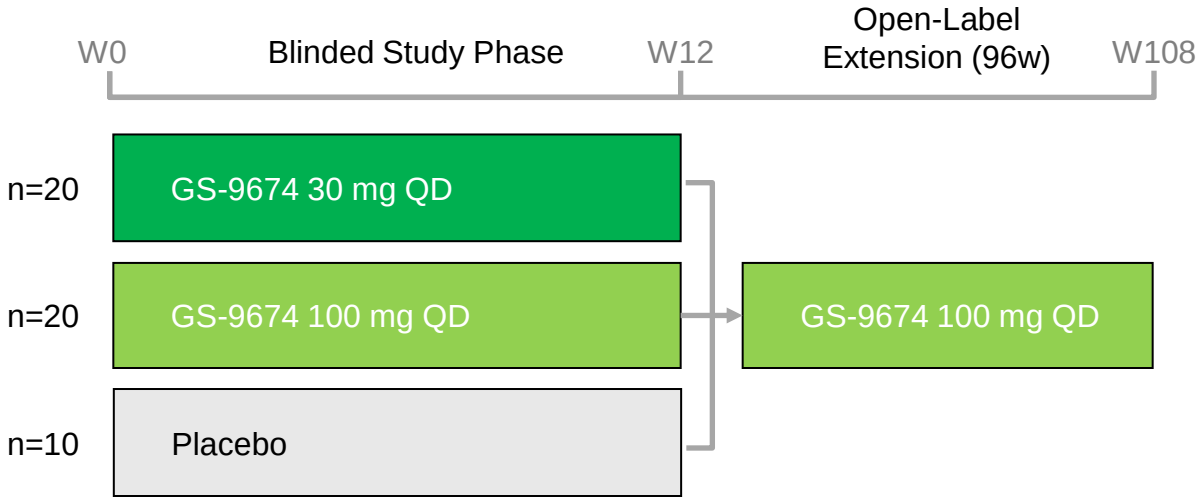
Primary Reasons for Screen Failure (21%)

- 235 patients enrolled of 298 screened

	Screen Failures (n=63)
Did Not Meet Eligibility Criteria	52 (83%)
Liver biopsy not consistent with PSC	16 (31%)
Active UC	8 (15%)
Unwilling/unable to comply with study procedures	7 (14%)
History of decompensation	5 (10%)
Willing/able to consent	4 (8%)
MRPC not consistent with PSC	3 (6%)
Ascending cholangitis within 60 days	3 (6%)
Compliance concerns	3 (6%)
Met Eligibility Criteria, But Not Enrolled	11 (18%)
Outside of window	6 (55%)
Investigator discretion	2 (18%)

Muir AJ, et al. EASL 2017.

GS-9674 for PSC: Phase 2 Study Design



Endpoints

1. Safety
2. Improvement in liver biochemistry (ALP)
3. Improvements in QoL

Purpose: To determine the safety, tolerability, and efficacy of GS-9674 in patients with PSC.

Population: Non-cirrhotic PSC (cholangiography)
ALP >1.67x ULN

GS-9674 for PSC: Inclusion/Exclusion Criteria

Major Inclusion Criteria

- 18-70 years
- PSC on cholangiogram within 12 months
- Serum ALP >1.67 x ULN
- Stable UDCA for 12 months
- Stable immunosuppressants for 3 months
- FibroTest <0.75 (to exclude cirrhotics)
- Platelets ≥150,000
- Albumin ≥3.3 g/dL
- Creatinine <ULN
- If IBD+, no evidence of active IBD on colonoscopy within 6 months

GS-9674 for PSC: Inclusion/Exclusion Criteria

Major Exclusion Criteria

- ALT > 10x ULN
- Bilirubin >2x ULN
- INR >1.2 (unless anti-coagulated)
- Cirrhosis (biopsy, prior decompensation, or Fibroscan >14.4 kPa)
- Small duct PSC
- Other causes of liver disease
- + AMA
- Liver transplantation
- Prior HCC or cholangiocarcinoma (if dominant stricture, cholangiocarcinoma must be ruled out prior to randomization)
- Cholangitis within 60 days of screening
- Indwelling stent
- Active IBD (partial Mayo score >1, rectal bleeding score >0)
- Antibiotics for the treatment of PSC (e.g. vancomycin)

Primary Reasons for Screen Failure (10%)

- 52 patients enrolled of 57 screened
  - Significant pre-screening activity (ALP, IBD, UDCA use)

- Primary reasons for failure
  - ALP too low
  - No cholangiographic diagnosis within 12 months
  - Unstable UDCA dose
  - Active IBD
  - Prohibited concomitant medication

Patient Retention in Phase 2 SIM Study

- Highly motivated patient population
- 83% completed 2-year study
- Reasons for withdrawal
  - AEs (8%)
  - Withdrawal of consent (6%)
  - Protocol-specified reason (2%)
- Liver biopsy availability
  - 91% at Week 48
  - 81% at Week 96

Muir AJ, et al. EASL 2017.