Ipsen Clinical Trials Update: Primary Sclerosing Cholangitis

Benjamin Miller, PharmD
Vice President, Liver Portfolio Development Lead

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IPSEN

Ipsen is dedicated to creating better outcomes and transforming the outlook for people living with rare liver disease

Our current rare liver disease focus areas are:

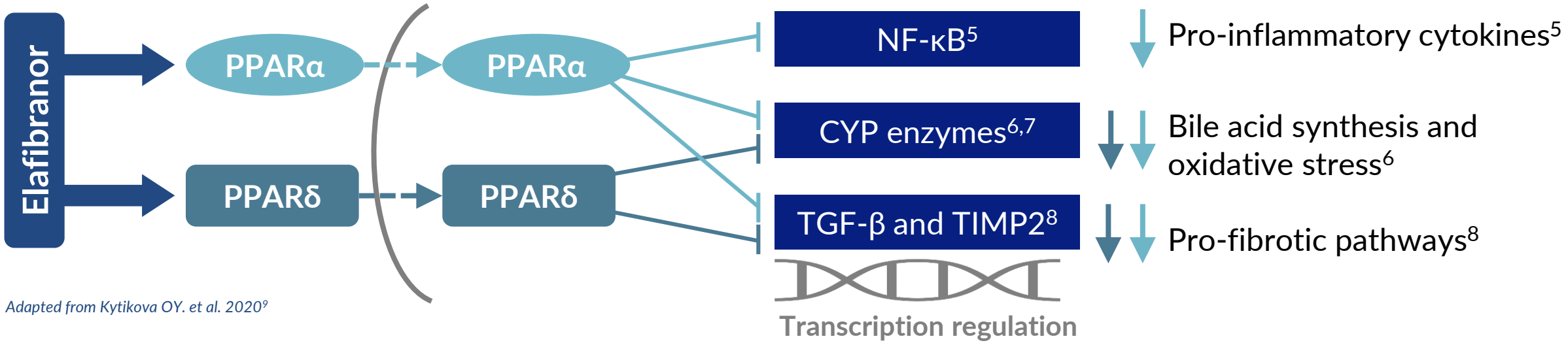
- ***Primary Sclerosing Cholangitis (PSC)***
- Primary Biliary Cholangitis (PBC)
- Progressive Familial Intrahepatic Cholestasis (PFIC)
- Alagille Syndrome (ALGS)
- Biliary Atresia (BA)

The purpose of this presentation is to provide an overview of Ipsen clinical trials for PSC in response to a request from the PSC Partners Seeking a Cure organization.

The safety and efficacy of elafibranor and ritivixibat in PSC are currently being investigated and are not approved by the FDA

Background on elafibranor

- Elafibranor is an orally administered PPARα/δ agonist[1]
- Dual activation of PPARα and PPARδ may function synergistically in PSC[2-4]



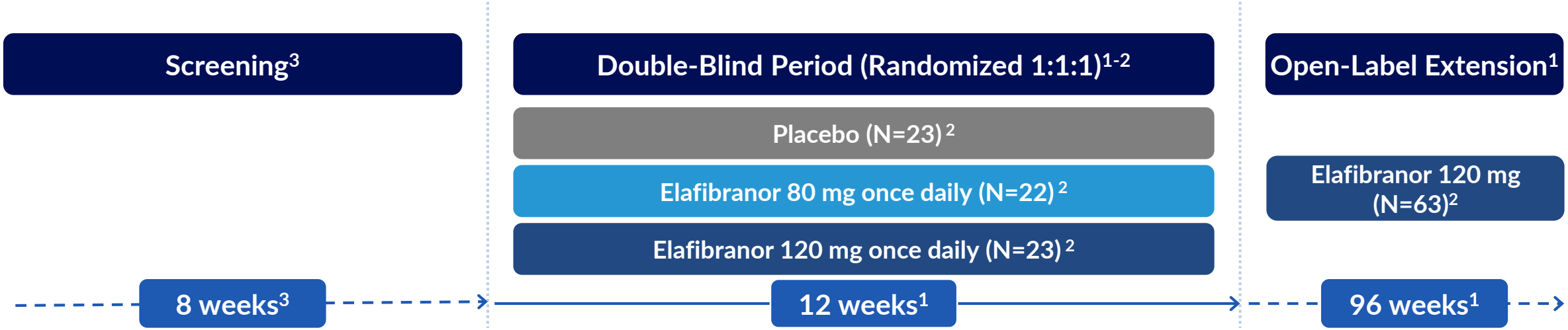
Adapted from Kytikova OY. et al. 2020[9]

The safety and efficacy of elafibranor in PSC is currently being investigated and is not approved by the FDA.

1. Kowdley KV, et al. *N Engl J Med*. 2024;390:795–805. **2.** Pawlak M, et al. *J Hepatol*. 2015;62:720–733. **3.** Christofides A, et al. *Metabolism*. 2021;114:154338. **4.** Kersten S, et al. *Biochimie*. 2017;136:75–84. **5.** Grabacka M, et al. *Int J Mol Sci*. 2021;22:10545. **6.** Gallucci GM, et al. *Cells*. 2024;13:1296. **7.** Kouno T, et al. *J Biol Chem*. 2022;298:102056. **8.** Staels B, et al. *Hepatology*. 2013;58:1941–52. **9.** Kyitkova OY, et al. *PPAR Research*. 2020:8906968. CYP, cytochrome P450; NF-κB, nuclear factor kappa-light-chain-enhancer of activated B cells; PPAR, peroxisome proliferator-activated receptor; PSC, primary sclerosing cholangitis; TGF-β, transforming growth factor beta; TIMP2, tissue inhibitor of metalloproteinases 2.

ELMWOOD: an ongoing phase 2 study of elafibranor in PSC (NCT05627362)

- ELMWOOD is a multinational, randomized, double-blind, placebo-controlled 12-week study that evaluated the effect of two doses of elafibranor (80 mg or 120 mg) compared to placebo[1]
- This study was designed with input and collaboration from patients living with PSC and included 68 patients from 62 sites worldwide[1]
- **Status (NCT05627362)**: the 96-week open-label extension is ongoing but not recruiting, with an estimated completion in 2026[1]

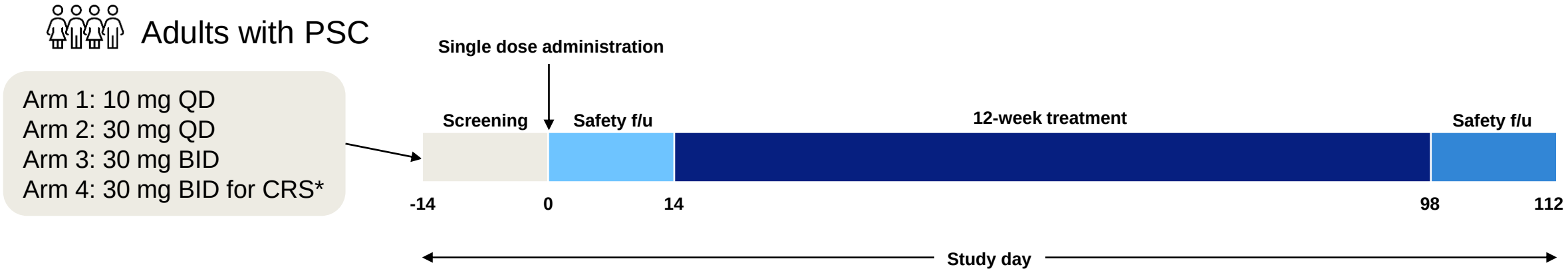


The safety and efficacy of elafibranor in PSC is currently being investigated and is not approved by the FDA.

1. ClinicalTrials.gov. "A Study to Assess Safety and Effectiveness of Elafibranor in Adult Participants With Primary Sclerosing Cholangitis. (ELMWOOD)." Availably at: https://clinicaltrials.gov/study/NCT05627362. Last accessed: 10 September 2025. **2.** Levy C, et al. Safety and efficacy of elafibranor in primary sclerosing cholangitis: The ELMWOOD phase II randomized-controlled trial. J Hepatol. 2025 May 8:S0168-8278(25)00252-1. doi: 10.1016/j.jhep.2025.04.025. Epub ahead of print. PMID: 40350321. **3.** J Hepatol. "Safety and efficacy of elafibranor in primary sclerosing cholangitis: The ELMWOOD phase II randomized-controlled trial: Supplementary data: Multimedia component 4." Availably at: https://www.journal-of-hepatology.eu/article/S0168-8278(25)00252-1/fulltext. Last accessed: 10 September 2025.

Ritivixibat: an orally administered, systemically bioavailable apical sodium-dependent bile acid transporter (ASBT) inhibitor

- The safety and tolerability of repeat administration of once or twice daily doses of ritivixibat was studied in a phase II, single-arm, open-label 12-week study in adults with PSC. This study included 18 patients at 8 sites in Europe (across Spain, France, Italy and Poland)
- Biomarkers of disease activity and serum bile acid levels will also be evaluated
- **Status (NCT05642468)**: study was completed in July 2025, results not yet available



The safety and efficacy of ritivixibat in PSC is currently being investigated and is not approved by the FDA.

ClinicalTrials.gov. "Safety and tolerability of A3907 in primary sclerosing cholangitis." Availably at: https://clinicaltrials.gov/study/NCT05642468. Last accessed: 11 Aug 2025. BID: twice daily; CRS: clinical relevant stricture; f/u: follow-up; QD: once daily.

Thank You