RELATE PBC Request for Proposals:

REaL-world treAtmenT with sEladelpar for PBC

Primary biliary cholangitis (PBC) is a chronic, autoimmune cholestatic liver disease characterized by progressive destruction of bile ducts that can lead to cirrhosis, liver failure, and in severe cases, patient mortality[1,2]. PBC patients often suffer from debilitating symptoms, such as pruritus and fatigue, and an overall decline in quality of life[1,2]. The reported prevalence varies worldwide (estimated 1.91 to 40.2 cases per 100,000 individuals) and predominately impacts middle-aged women[3,4].

Although ursodeoxycholic acid (UDCA) is the first line treatment for PBC, according to the AASLD PBC Practice Guidelines, up to 40% of patients fail to achieve an adequate biochemical response, which is associated with worse outcomes[1,5,6,7]. Moreover, many patients continue to endure severe symptoms, such as pruritus and fatigue[1,8]. Thus, there is a need for additional treatment options, especially amongst patients that fail to achieve an adequate response to UDCA.

Seladelpar[†] is a first-in-class PPAR-delta agonist (peroxisome proliferator activated receptor delta [PPARδ]) targeting multiple cell types implicated in the pathobiology of PBC with anticholestatic, anti-inflammatory, and antipruritic properties[9,10]. Based on the results of the Ph3 RESPONSE study, seladelpar was approved in the United States and United Kingdom for the treatment of PBC in combination with UDCA in adults who have an inadequate response to UDCA, or as a monotherapy in patients unable to tolerate UDCA[11*].

To better understand the real-world clinical experience with seladelpar, Gilead is launching the RELATE PBC request for proposals (RFP). The program will provide individual proposals with research support. Proposals submitted to the RFP should include studies with the following characteristics: clear objectives, data analysis plans with sufficiently robust sample sizes, defined timelines, a comprehensive operational plan, data that is relevant to the PBC community (including healthcare providers, patients, and caregivers), and plans for the data to be submitted to relevant congresses and journals. The program is open to applications in any regions where seladelpar is approved and commercially available for treatment of PBC.

RFP Research Topics

Gilead will evaluate and support select proposals aimed at addressing the following research topics with respect to routine clinical practice using seladelpar for the treatment of PBC:

1. Determine the real-world effectiveness and tolerability (including long-term) of seladelpar based on biochemical measures of cholestasis, liver injury, or inflammation and non-invasive tests (e.g. liver stiffness measures)
2. Evaluate the impact (including long-term) of seladelpar on patients living with PBC, e.g. symptoms (especially, pruritus and fatigue), quality of life, and activities of daily living
3. Characterize effectiveness and tolerability of seladelpar across a broad range of patients, including (but not limited to):
    a. Different genders, races/ethnicities, and socioeconomic status

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b. Varying clinical presentations: including, but not limited to, disease severity (e.g. early vs advanced ALP levels or fibrosis status), liver comorbidities (e.g. MASLD, MASH, AIH, ALD) [§], extrahepatic PBC manifestations (e.g. metabolic bone disease, hypercholesterolemia), other comorbidities (e.g. diabetes), or different treatment histories

RFP Application Criteria

- Both investigator-sponsored research (ISR) study proposals and collaborative research study proposals (developed in conjunction with Gilead) will be considered (link to additional information on ISR vs collaborative studies)
- Letters of Intent (LOIs) will only be reviewed in countries where seladelpar is commercially available and has regulatory approval for the treatment of PBC
- Proposed research endpoints should be based on sound scientific hypotheses and generalizable across countries/regions
- For studies that include patients based in Europe or the UK: Research questions related to tolerability should be included as secondary or exploratory analyses and not the primary study objectives
- Research proposals should include a comprehensive publication plan to present study results at scientific forums and to publish results in peer reviewed journals
- The proposed budget should be appropriately proportional with the study's scope
    - The proposed budget should include overhead costs and applicable taxes; overhead costs should not exceed 30% of the total budget
- The proposed study design should be feasibly executed within a reasonable timeframe proportional to the study's follow-up duration
- There must be no more than one sponsor for contract negotiations and/or Institutional Review Board (IRB) review
- As the study sponsor, the principal investigator will be responsible for compliance with all laws and regulations applicable to research sponsors, including satisfying local requirements and obtaining all necessary regulatory and ethical approvals before beginning the study

Application Process

To apply for consideration for funding under the RELATE PBC RFP Program, you will need to submit a LOI** that is no longer than two pages, contains a concise overview of the proposed project and includes the total estimated budget. Applicants should submit the LOI application in the Gilead Optics portal

How to Submit an LOI in G. OPTICS for the RELATE PBC RFP

- Create an account or log into your account in G. OPTICS.
- Select "New Letter of Interest (LOI)."
- Select "PBC: RELATE PBC RFP" from the list of active RFPs.
- Complete the required fields.
- Submit the LOI.

Gilead will evaluate and rank all letters of intent (LOIs) received on a rolling basis until funds are exhausted.

- Submission window opens February 6th, 2025, at 00:00
- Submission window closes April 3rd, 2025 at 23:59

Questions about the RFP or the application process can be submitted to your local Gilead Medical Science Liaison. A review of the LOIs will result in invitations for selected LOI applicants to submit a full proposal with a detailed budget.

LOIs will be rigorously reviewed by a Gilead internal committee. Each complete LOI that meets program requirements will be assigned to multiple reviewers. Each reviewer will review the LOI and evaluate how well the proposal addresses the RFP, the potential impact of the study, the strength of the objectives/study design, sustainability/scalability of the proposal/intervention, and the site's and study team's ability to recruit the proposed study population and execute on study objectives. Investigators with the top submissions will be offered the opportunity to submit a full application including a detailed budget, adequate and proportional to the study's scope, which will be similarly reviewed.

Gilead's approval of awards will depend on the availability of funds and receipt of meritorious and complete proposals. Awards shall be granted solely on the merit of the research and alignment with the criteria of this program.

No Guarantee of Funding

Gilead reserves the right to approve or decline any proposal at its sole discretion. Submission of an LOI or a full proposal does not guarantee funding.

Awards shall be for research purposes only; routine medical care or other costs associated with routine medical care will not be considered for funding.

No Inducement or Reward

Gilead approval of awards does not take into account the past, present, or future volume or value of any business or referrals between the parties. Awards are not being given, directly or indirectly, as an inducement or reward with respect to the past or potential future purchase, utilization, recommendation or formulary placement of any Gilead product. Furthermore, except for the use of the Gilead product in an approved award/research, the awardee is not required to purchase, order, recommend or prescribe to any patients any products manufactured by or available through Gilead.

About Gilead Sciences

Gilead Sciences, Inc. is a biopharmaceutical company that discovers, develops and commercializes innovative therapeutics in areas of unmet medical need. The company's mission is to advance the care of patients suffering from life-threatening diseases worldwide. Gilead has operations in more than 30 countries worldwide, with headquarters in Foster City, California.

References

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Footnotes:

†Seladelpar refers to Gilead's Livdelzi®. Livdelzi was granted accelerated approval for the treatment of PBC by the U.S. Food and Drug Administration (FDA) in August 2024. Livdelzi was granted UK marketing authorization for the treatment of PBC by the UK Medicines and Healthcare Products Regulatory Agency (MHRA) in January 2025. Seladelpar received FDA Breakthrough Therapy Designation, as well as Orphan Drug Designation for the treatment of people living with PBC. Seladelpar has Priority Medicine (PRIME) designation in the EU, which is assigned to optimize the development of novel medicines that target conditions with an unmet medical need for which no treatment options exists or where they can offer a major therapeutic advantage over existing treatments.
As part of the FDA accelerated approval, Gilead has committed to a confirmatory long-term outcomes study called AFFIRM, which has already been initiated in people with compensated cirrhosis. Continued U.S. approval may be contingent upon verification of clinical benefit in confirmatory trial(s).
More information concerning US Prescribing Information for Livdelzi is available here.
More information concerning the UK MHRA Summary of Product Characteristics (SmPC) is available here

**As of January 2025, seladelpar remains under regulatory review with regulatory agencies and has not obtained market authorization for the treatment of PBC in any country outside the US and UK*

§ MASLD: metabolic dysfunction-associated steatotic liver disease; MASH: metabolic dysfunction-associated steatohepatitis; AIH: autoimmune hepatitis; ALD: alcohol-related liver disease

***LOIs are not binding documents for either party. The purpose of the LOI is a brief summary of the proposed study to enable Gilead to determine on a preliminary basis whether the proposed study and related budget are aligned with the criteria, timeline, and scope of this RFP.*