PSC Partners Research Programs: The Evolving Role of the Patient In Clinical Research

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PSC Partners Seeking a Cure

Evolving Role of the Patient
In Rare Disease Clinical Research

Patient Targeted	**PATIENT AS A CONSUMER** • Market research and DTC advertising • Recruitment and participation in trials
Patient Centered	**PATIENT AS A STAKEHOLDER** • CABs, Steering Committees • Input into protocol design and community education on research
Patient Partnered	**PATIENT AS A CO-CREATOR** • Participation in every step of development • Venture philanthropy
Patient Led	**PATIENT AS A LEADER** • 360-degree oversight of a study or research program • Non-Profit Drug Company

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PSC Partners Clinical and Research Activities

- 19 conferences in collaboration with top PSC academic centers
- Awarded $6M+ for 111 international PSC research grants
- Collaborating with biotech/pharma companies to support protocol review, trial recruitment and patient education
- IRB-approved Patient Registry (2,600+ participants)
- PSC-specific ICD-10 code in 2018
- Patient Focused Drug Development Forum with FDA
- Chan Zuckerberg Initiative Grants
  - Rare as One Grant
  - Single-Cell Patient Partnered Collaborative Grant with Sonya MacParland

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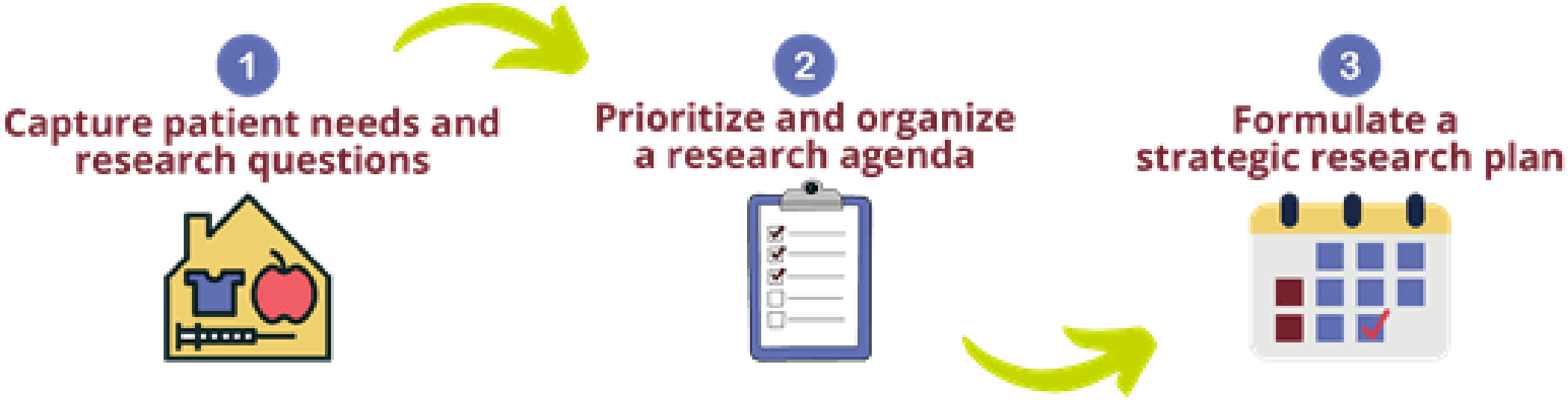
PSC Partners Strategic Research Plan



- Incorporated the voices of more than 500 PSC patients and caregivers
- More than 100 patients and caregivers participated in 15 focus groups
- A total of 65 community and 59 researcher recommendations across 6 topics
- Community/Researcher alignment identified 22 (37%) recommendations
- Process being presented at TLM 2023 on Saturday (Poster # 3784-C)

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PSC Partners Strategic Research Plan
Focused PSC Research Pathways

- Assessment of multi-stakeholder recommendations formed pillars of focus for the structure of PSC Partners Strategic Research Plan

1. ***Improve understanding of the mechanisms contributing to the development and progression of PSC***
2. ***Further understanding of the gut-liver connection in PSC.***
3. ***Develop safe and effective treatments to slow progression and reduce symptom burden.***

- All programs should include community support and education through patient engagement and knowledge translation.

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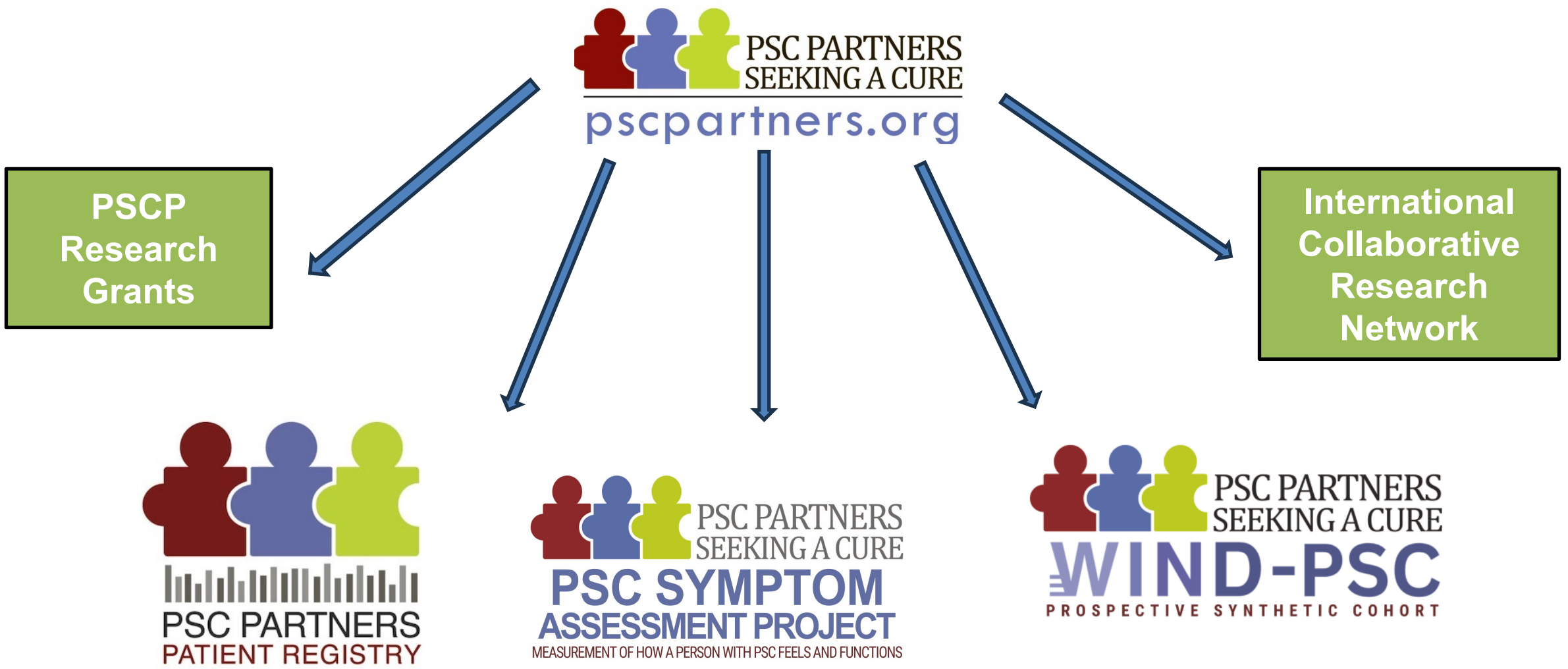
PSC Partners Strategic Research Plan
Putting the Plan into Action



WIND-PSC
Study Objectives

Primary

- Develop an appropriate real-world data comparator cohort to support the design and execution of interventional studies and serve as an external control for interventional clinical trials in PSC

Secondary

- Develop a large clinical and biomarker data set to identify individual and/or composite surrogate endpoints likely to predict clinical benefit for use in the design of interventional studies in PSC
- Evaluate patient reported symptoms, quality of life, and other direct patient experiences through standardized tools to determine the association between patient symptoms over time with clinical markers and disease progression

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WIND-PSC
Study Design Overview

- WIND-PSC is a global, prospective, multi-center, observational cohort with patients followed up to 5 years
- Approximately 2000 patients will be enrolled at up to 15 sites in North America and Europe
- Primary clinical endpoints are liver disease progression
- Patients will be assessed onsite annually with physical exam, labs, imaging, liver stiffness, and fibrosis biomarkers
- Clinical symptoms and events (“safety”), medications, procedures, and patient reported PSC symptoms will be assessed quarterly

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WIND-PSC
Key Enrollment Criteria

- Overall population targeted to be representative of the PSC population(s) enrolled in late-stage clinical trials
- Inclusion criteria
  - Adult patients with large duct PSC
  - Patients with compensated cirrhosis, features of AIH,
  - Stable PSC and IBD therapies
- Exclusion criteria
  - Small duct PSC
  - History or current evidence of decompensated cirrhosis
  - MELD >15, listed for transplant or prior transplant
  - Hepatobiliary malignancies
  - Participation in other interventional clinical trials

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WIND-PSC
Key Clinical and Biomarker Data

- Patient demographics, PSC and IBD disease and treatment history
- Liver biochemistries and other standard of care labs
- PSC- and IBD-related procedures
- Transient elastography (routine) and other imaging (as available)
- Safety events
- Concomitant medications
- PROMs for key symptoms
- ELF, PRO-C3
- Three exploratory biomarker samples stored for future research

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Unique Study Design vs Natural History Cohorts

- Primary endpoints consistent with current guidance for chronic liver disease (decompensation, hepatobiliary malignancies, transplant, death)
- Alignment with FDA Guidance for RWE/RWD
- Standardized clinical safety collected, graded for severity and relationship to PSC, and MEDRA coded
- Independent adjudication of liver-related outcomes events and SAEs
- Concomitant medications collected similar to clinical trials
- PROMs for key symptoms and QoL
- 21 CFR Part 11 and GDPR compliant data system
- Sites monitoring by a CRO with 100% source data verification

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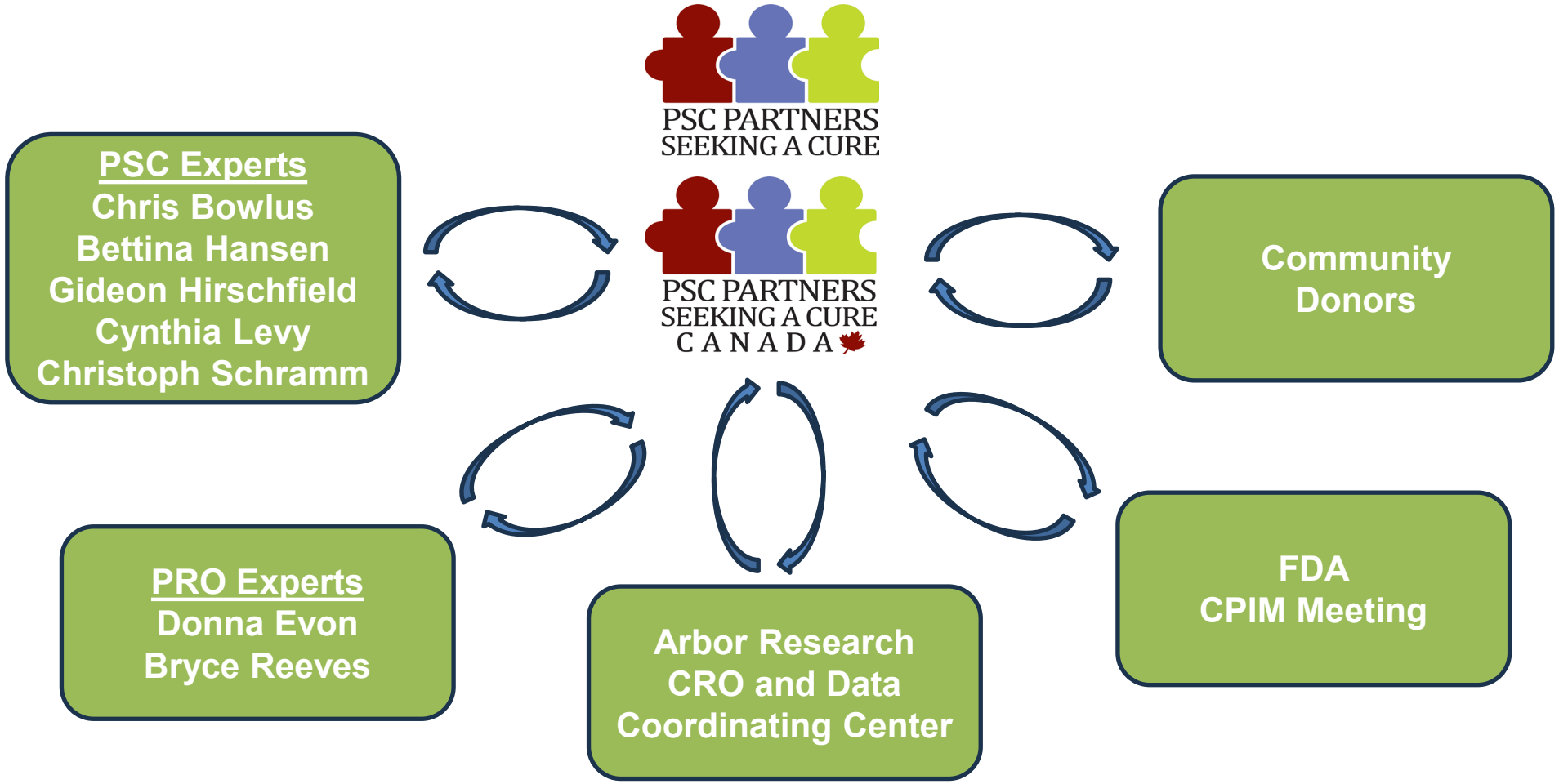
WIND-PSC
Patient-Led Collaborative Effort

First Patients Targeted for Enrollment in Q1 2024



International Collaborative Research Network Expansion of PSCP Research Strategy

- Scientific convening of 56 PSC researchers from USA, Canada and Europe over 2 days
- Chaired by Chris Bowlus and Josh Korzenik and sponsored by PSC Partners and Resnek Family Center for PSC
- Primary goals
  - Provide a collaborative forum to share latest research and prioritize unaddressed or evolving research questions
  - Develop and prioritize potential research proposals than align with PSC Partners Research Strategy for potential sponsorship
  - Establish a network of collaborative researchers and foster new connections for collaborations outside ICRN

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ICRN Meeting and Working Groups

- General Session with state-of-the art lectures relevant to each WG
- Three Breakout Sessions
  - Research Presentations
  - Discuss key research questions and unmet needs
  - Identify potential projects for further development
- Summary presentations from each WG

PATHOPHYSIOLOGY	GUT-LIVER AXIS	DIAGNOSIS AND PROGNOSIS	CLINICAL TRIALS AND ENDPOINTS
Michael Trauner Sonya MacParland	Johannes Hov Josh Korzenik	David Assis David Goldberg	Chris Bowlus Stephen Rossi

- Each working group was comprised of researchers with relevant expertise
  - Hepatologists and IBD experts (adult and pediatric)
  - Basic scientists
  - FDA and NIH
  - Patient representatives

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Diagnosis and Prognosis WG

- Further validation of the detection of proteins carried in extracellular vesicles for early CCA diagnosis within WIND-PSC cohort
- “Pre-PSC” study
  - Follow patients with IBD and collect samples until PSC develops
  - Compare the IBD patients that develop PSC to those that do not
- “Recurrent-PSC” study
  - Follow patients with PSC who had a liver transplant
  - Compare the patients with recurrent PSC vs. no recurrence
  - Identify differences in immunology, microbiome, etc. that correlate with developing PSC in both populations

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Clinical Trials and Endpoints WG

- Integration of global data for TE, ELF and PRO-C3 (?)
  - Analysis of existing data for TE and ELF to determine what is a clinically meaningful change
  - Identify blood samples available for measuring ELF
  - All data analysis needs to meet regulatory standards
  - Data will be integrated with prospective data from WIND-PSC
- PRO assessment of patients diagnosed and/or treated for acute cholangitis or “flare”
- Standard definition of acute cholangitis for potential endpoint and comparison to PRO data => PSC Forum Project

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Gut-Liver Axis WG

- A prospective cohort of individuals with a diagnosis of PSC to collect stool and blood initially
  - Include healthy controls and patients with and without UC
  - Understand bile metabolism using stool/plasma + microbiome WGS/metabolomics of stool and plasma with bile profiling
  - Collaborate and enhance WIND-PSC data set
- A prospective cohort of individuals with UC followed prospectively prior to development of PSC
  - Collect similar samples to better characterize early-stage disease
  - Collaborate with CCF and SPARC trial

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Pathophysiology WG

- Establishment of a PSC-specific preclinical pipeline via the formation of a consortium for research.
- Steps in the pipeline, including model development, new drug discovery, and drug repurposing
- Collaboration with the National Center for Advancing Translational Sciences (NCATS) at the National Institutes of Health (NIH).
- A proposed timeline of 4 years, including phases for gap analysis, collaboration, data collection, and model development.

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ICRN – Next Steps

- Further develop abbreviated research project proposals
- Expand the WG members to broaden expertise
- Steering committee will include co-chairs and PSC Partners representatives
- Regular meetings of WG to establish project teams and develop full proposals
- Project proposals will be shared with the patient community to prioritize which projects PSC Partners will look to support
- Second annual meeting targeted for late 2024

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Thank You!

- PSC Partners Staff, Volunteers and Board Members
- Scientific Medical Advisory Committee
- Clinicians and researchers
- Industry partners
- **PSC Patients, Caregivers, Family and Friends**

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