PVRI **Innovative Drug Development Initiative (IDDI) Report 2018**



Peter Fernandes, Sylvia Nikkho & Paul Corris

The Pharma Task Force was established in January 2017 and has made an energetic start under the leadership of Sylvia Nikkho (Bayer), Peter Fernandes (Bellerophon) and Paul Corris (PVRI).

It is a vibrant discussion forum which addresses much needed questions surrounding the future of trials comprising novel drugs. Since its establishment, it has developed a good rapport with regulatory bodies, such as the European Medicines Agency (EMA) in Europe and the Food & Drug Administration (FDA) in the United States.

The Task Force has established three workstreams - endpoints, clinical trial design, biomarkers - which are interlinked and mutually supportive.

Thanks to the dedication of the leaders, the Pharma Task Force has gained momentum and strength, which has led the PVRI to embed it within its four strategic backbone initiatives. To that effect, and to better reflect its purpose and activities, the Task Force was renamed the **Innovative Drug Development Initiative (IDDI).**

The three IDDI workstreams, each led by an academic and a pharma representative, are:

1 **Clinical Trial Endpoints** led by:
// Olivier Sitbon (University Paris-Sud, France)
// Sylvia Nikkho (Bayer, Germany)

2 **Clinical Trial Design** led by:
// Jim White (University of Rochester, USA)
// Peter Fernandes (Bellerophon, USA)

3 **Biomarkers** led by:
// Anna Hemnes (Vanderbilt University, USA)
// Lawrence Zisman (Gossamer Bio, USA)

Activities during 2018

Face-to-face meetings were held throughout the year. These were well attended with over 20 representatives from academia, patient organisations, regulatory agencies and the pharma industry at each meeting. Presentations and stimulating discussions were held at each of the following:

- **January:** PVRI Annual World Congress, Singapore
- **July:** PVRI Drug Discovery & Development Symposium, Bethesda, USA
- **September:** ERS Conference, Paris, France.

In addition, regular telephone conference calls were held throughout the year.

PVRI IDDI Structure

PVRI IDDI Leaders

Peter Fernandes Bellerophon, USA	**Paul Corris** Newcastle University, UK	**Sylvia Nikkho** Bayer, Germany

Workstream Leads

CLINICAL TRIAL DESIGN


Jim White University of Rochester, USA

Peter Fernandes Bellerophon, USA

CLINICAL TRIAL ENDPOINTS


Olivier Sitbon University Paris-Sud, France

Sylvia Nikkho Bayer, Germany

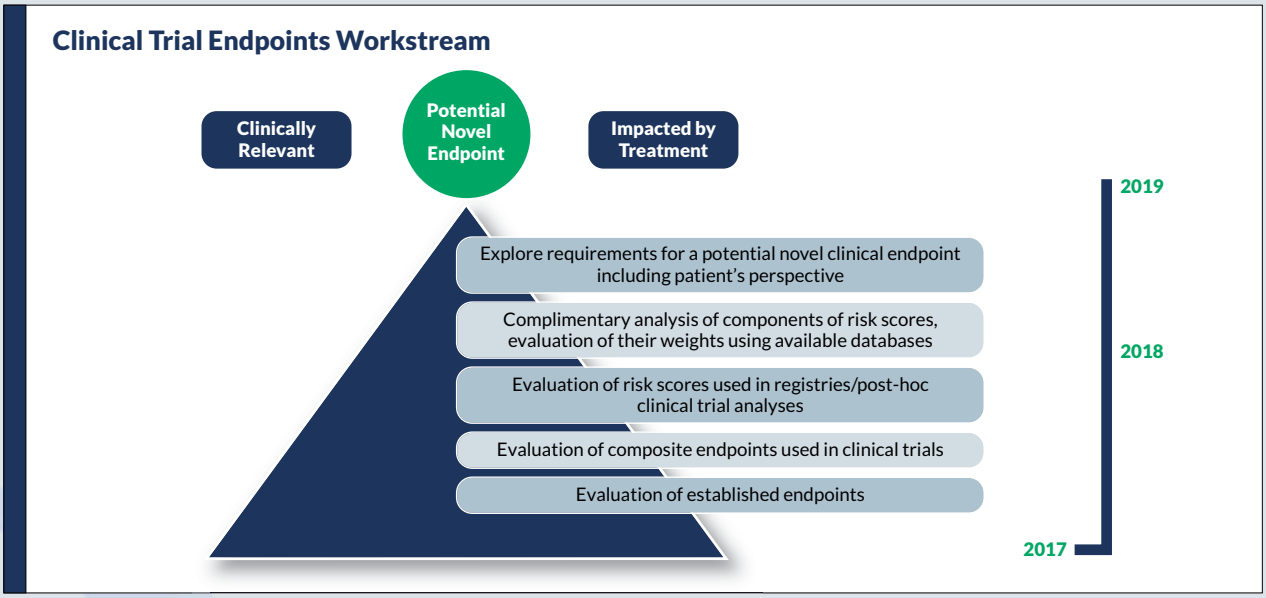
BIOMARKERS


Anna Hemnes Vanderbilt University, USA

Lawrence Zisman Gossamer Bio, USA

Clinical Trial Endpoints Workstream

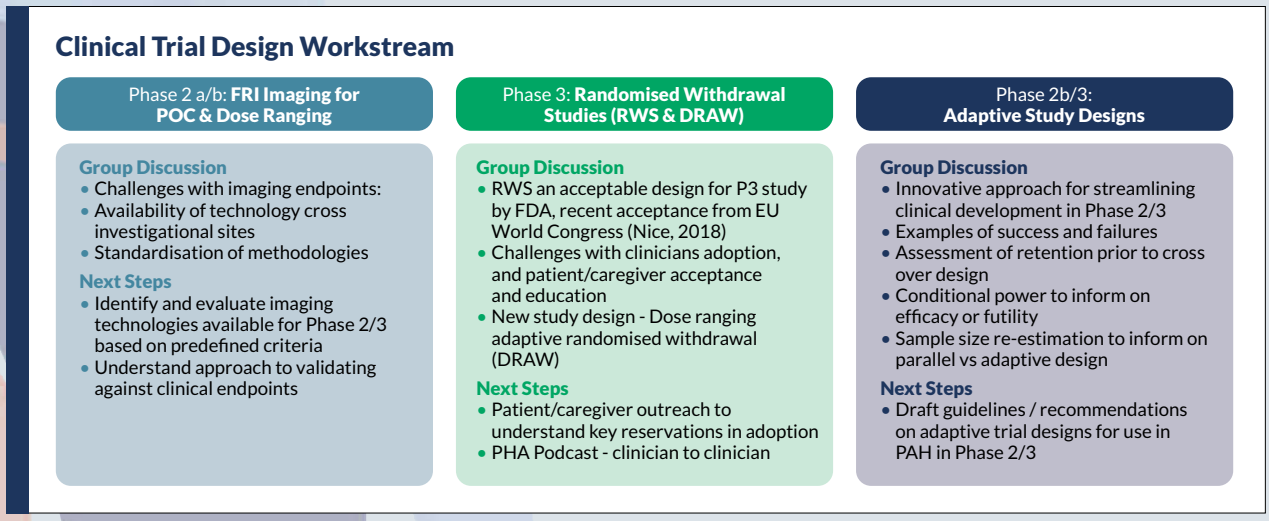
Under the leadership of Olivier and Sylvia, discussions focused on the potential role of utilising risk scores as an endpoint in trials. Valuable input was provided by the group of Raymond Benza on new developments in machine learning via the Pulmonary Hypertension Outcome Risks Assessments (PHORA) project, which applies data to refine risk using a Bayesian statistical approach.



The workstream continues to assess already established and used composite endpoints in clinical trials. It is anticipated that discussions will continue relating to the choice of risk score in endpoints for both phase 2 and 3 trials with a presentation to be made at the PVRI Annual World Congress in Barcelona in January 2019 and at the PVRI Drug Discovery & Development Symposium, in Paris on 1-2 July 2019.

Clinical Trial Design Workstream

Under the leadership of Jim and Peter, three main topics were discussed during the year.



Future activities will focus on the role of innovative trial design, including the use of better stratification of patients at trial enrolment. Furthermore, enrichment strategies and an adaptive approach to trial design and withdrawal studies will be explored. The group is also working on a position paper, which will be published in collaboration with the other workstreams.

Biomarkers Workstream

Under the leadership of Anna and Lawrence, this workstream explores the rapidly developing scientific area. A kick-off meeting took place in August to consider the challenges of both clinical trial design and novel surrogate endpoints in phase 2 studies of anti-proliferative approaches.

Work continues on the following topics:

- Biomarkers predicted to play a more prominent role in future clinical trials
- Enrichment strategies: use in adaptive trial designs
- Surrogate Endpoints
- Repurposing
- Work product of Biomarker Group
- Integrate recommendations with Clinical Trials Endpoints working group
- Position paper: state the issues without necessarily resolving them
- Play a role in resource sharing
- Planned next steps:
- Regular telephone conferences
- Presentation of (interim) results at the PVRI Drug Discovery & Development Symposium, which will take place in Paris, France, on 1-2 July 2019.

Objectives for 2019

The goal of the IDDI for the next year is to give a presentation at the PVRI Drug Discovery & Development Symposium, summarising the output of each workstream. Subsequently, we aim to publish a position paper, including sections of all three workstreams in *Pulmonary Circulation*.

A note of thanks from the PVRI

We would like to express our sincere thanks to the dedicated leaders and all members of the IDDI. We greatly appreciate the support from all Roundtable members, who are part of the IDDI.

The PVRI delegates were touched by the Rand Family and their inspiring music 'Breathless on Broadway', which illustrated what it was like for patients and their family who suffer from pulmonary hypertensions. This musical interlude was organised by Peter Fernandes (co-chair of the IDDI) during the IDDI meeting in Bethesda, July 2018.