The Investigative Medicines Initiative (IMI2)

Liver Investigation: Testing Marker Utility in Steatohepatitis

Liver Forum NASH 2020 Updates, Webinar 11 Aug 2020

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Chair Work-Package 7, LITMUS

Prof Quentin M. Anstee PhD, FRCP

Project Coordinator (Newcastle University, UK)

Dr Julia Brosnan PhD

Project Lead (Pfizer, USA)

Disclosure Slide

IMI consortium activities

LITMUS, Work-package 7 co-lead – NASH biomarker development
EU-PEARL, Work-package 6 co-lead - NASH platform studies

Current position

Director Clinical Development Liver Disease (NASH),
General Medicine and Infectious Diseases, AbbVie/Allergan
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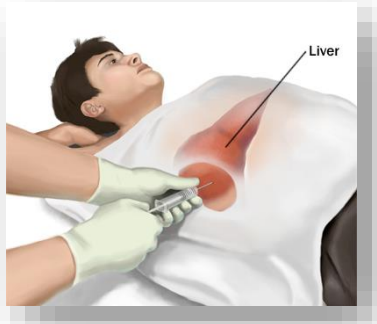
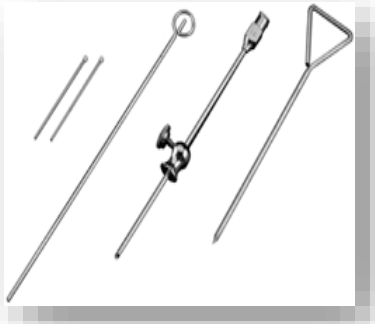
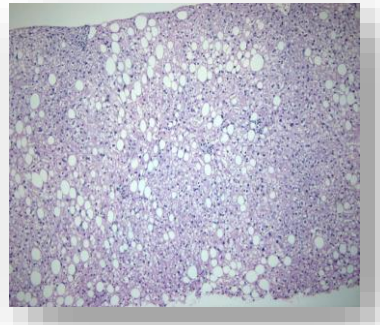
LITMUS: A Global Effort to Validate NAFLD/NASH Biomarkers

The overarching objectives of LITMUS are to develop, robustly validate and advance towards regulatory qualification biomarkers that diagnose, risk stratify and/or monitor NAFLD/NASH progression and fibrosis stage for use in drug discovery.







Diagnostic **Prognostic** **Monitoring**

LITMUS

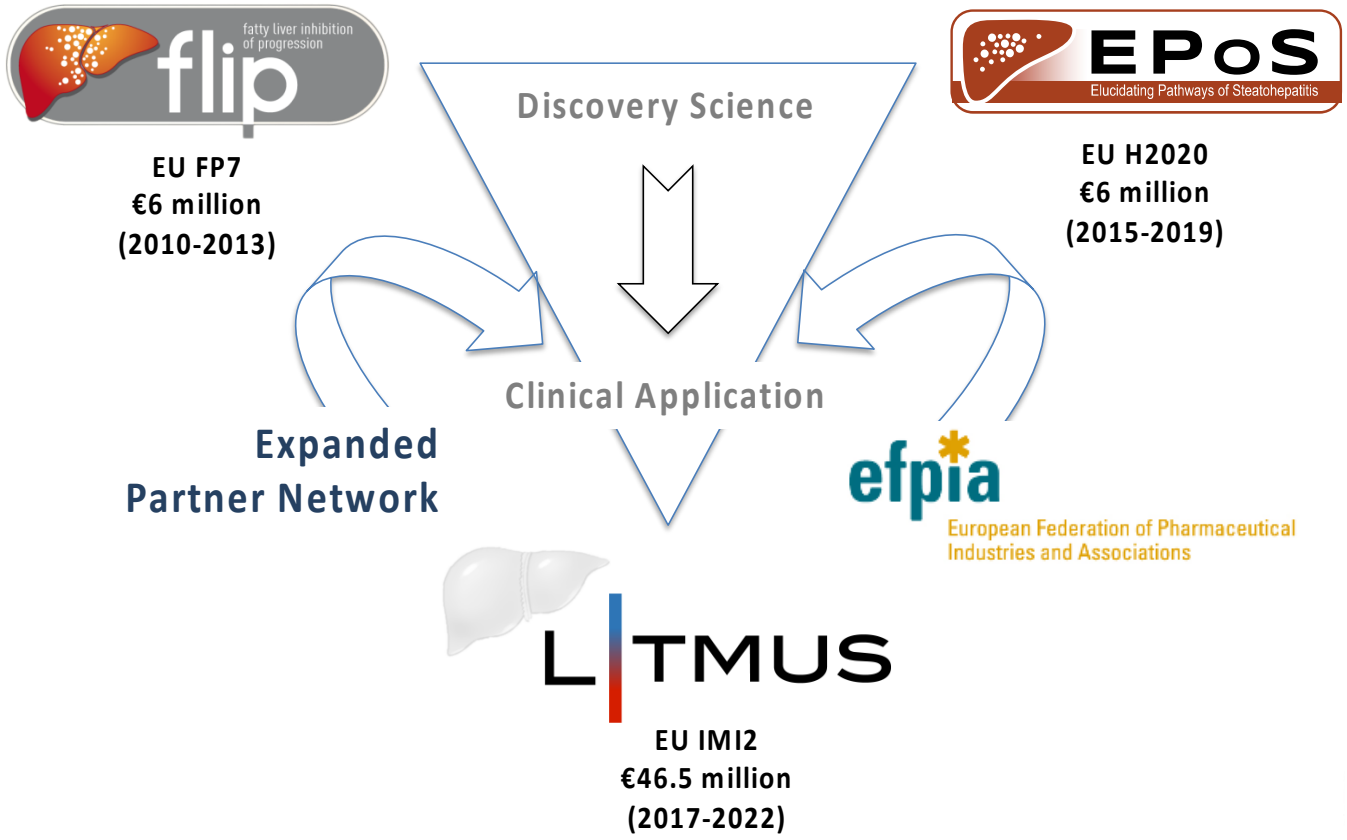
LITMUS (Liver Investigation: Testing Marker Utility in Steatohepatitis)

FACTS & FIGURES

Start Date	01/11/2017
End Date	31/10/2022
Call	IMI2 - Call 9
Grant agreement number	777377

Type of Action:
RIA (Research and Innovation Action)

Contributions	**€**
IMI Funding	15 797 881
EFPIA in kind	24 180 663
Other	6 483 232
Total Cost	46 461 776



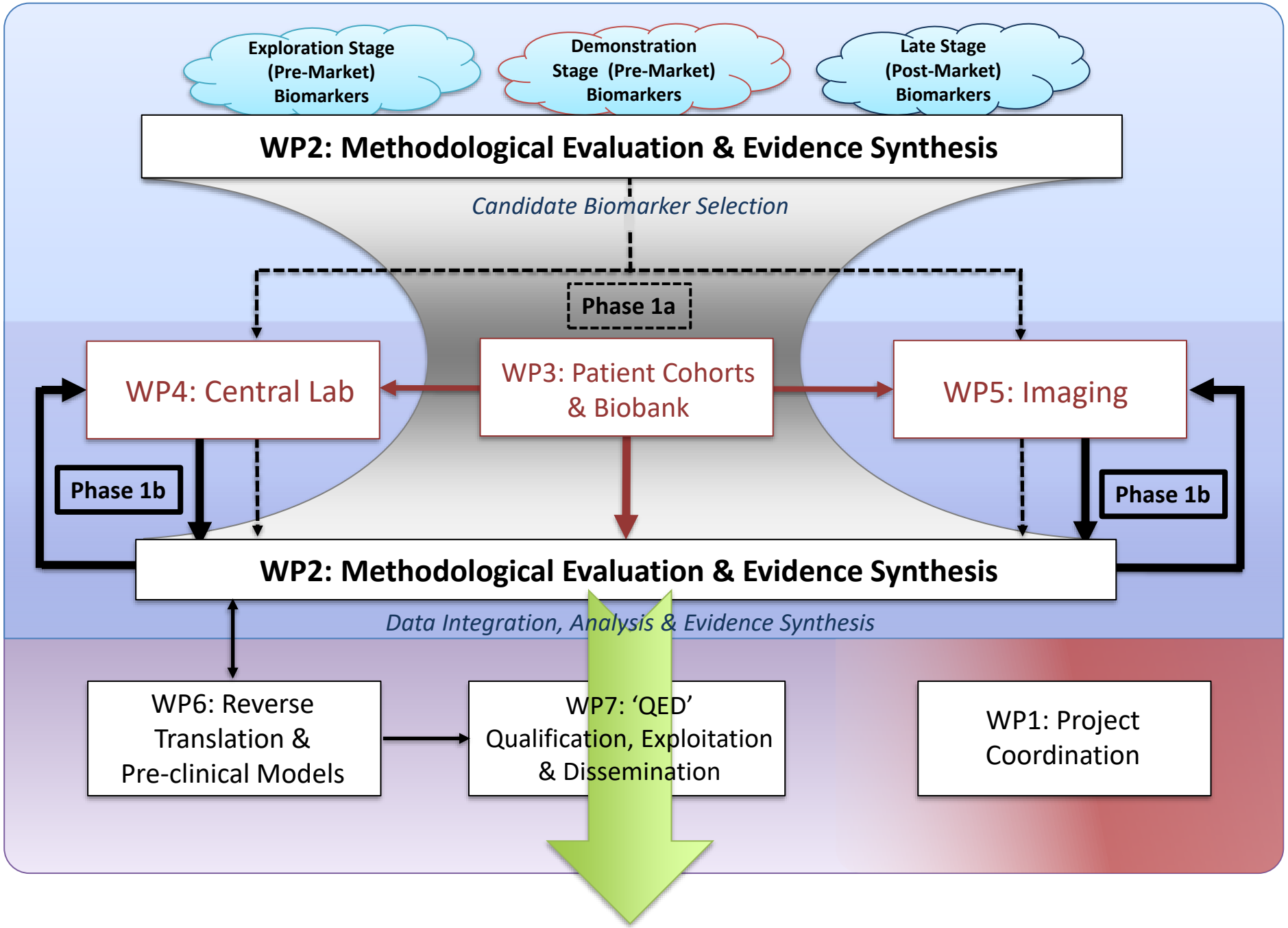
PROJECT LINKS

Project website: www.litmus-project.eu

Twitter: @LITMUS_IMI

Coordinator: Prof Quentin M. Anstee

The LITMUS Consortium comprises 53 Partners from 14 countries
29 Academic, 23 EFPIA/Industrial, 1 Professional body



Validated Diagnostic, Prognostic & Dynamic Biomarkers

Qualification strategy and status (WP7)

Richard Torstenson, for work-package 7

- Nordic Bioscience; Elisabeth Erhardtsen and Morten Karsdal,
- Takeda; Guido Hanauer, Novartis; Cliff Brass, Pfizer; Julia Brosnan
- Newcastle University; Quentin M Anstee, ICAN; Vlad Ratziu
- AMC; Patrick Bossuyt

Qualification strategy

Aim

Early authority feedback on the qualification feasibility and applicability of MetaCohort data (EPoS/FLIP) for exploratory work and the LITMUS trial for confirmation of the biomarker performance

Complexity

Several CoUs and several potential markers for each CoU

To optimize the qualification advice received

- 2 markers submitted for each CoU
- Both wet and imaging marker included

FDA

CPIM

Letter of Intent (LOI)

Qualification Package (QP)

Qualification (FQP)

Clinical data package

METACOHORT

Prospective data collection (EPOS/FLIP)

Biomarkers

- Retrospective analysis

Histology based diagnosis

- N ~ 1000 patients
  - F0-F4 ~20% each (centrally read)
  - Paired histology (appr 600)

Biomarker performance

LITMUS study

Prospective data collection (Protocol/code book)

Biomarkers

- Analysis: FDA standard (CSLI)

Histology based diagnosis

- N ~ 2000-2500 samples/patients
- Paired histology

PROs

Imaging data (substudy)

Confirmatory

Pharma-Data

Prospective data collection (DB clinical data)

Biomarkers

- In database
- Retrospective analysis possible

Histology based diagnosis

- N > 2000
- Paired histology

Allergan, AstraZeneca, Genfit, Gilead Intercept, Novartis

External validation

European - NAFLD registry

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LITMUS Progress Update – Qualification status

WP7: QED (Qualification, Exploitation & Dissemination)

EMA

Innovative Task Force (ITF) meeting

- Continue for a Qualification meeting

Qualification Advice

- Briefing package submitted for Diagnostic & Prognostic CoU
- 2 Scientific Advice face to face meetings
- Qualification Advice received

FDA

Critical Path Innovation Meeting (CPIM)

- Meeting not needed, submit LOI

Letter of intent (LOI)

- LOI submitted for Diagnostic & Prognostic CoU
  - Diagnostic LOI approved
    - https://www.fda.gov/media/138542/download
  - Prognostic LOI pending

Qualification Plan (QP)

- *pending selection of most promising marker*
  - *ongoing work in work-package 2*

Authority questions/topics of interest

Topics/Questions

- CoU description
- Applicability of data cohorts for each CoU
- Use of industry study data (external validation)
- Biomarker analytical stability
- Reference:
  - Histology assessment, standardised reading
- Statistical analysis
- Specific biomarker feedback

LITMUS Progress Update – Data Synthesis

WP2: Methodological Evaluation & Data Synthesis

Prioritising of markers for qualification

– **Systematic reviews**

- summarizing the existing evidence and utility for a range of “wet” and imaging biomarkers

– **Performance analysis ongoing**

- All LITMUS MetaCohort samples analysed for planned markers

In summary

- Positive authority feedback on LITMUS qualification strategy (FDA/EMA)
- Selection of most optimal marker for each CoU ongoing
- Next stage
  - submission of qualification package
  - analysing LITMUS study for confirmation of biomarker performance

New IMI2 "Restricted Call" for LITMUS follow-on project
Grant Submission deadline: 29th September 2020

MOSAICS

Mechanisms of Steatohepatitis: Artificial Intelligence & Clinical Science

Key Topic Areas for Research:

- **Extended follow-up of European NAFLD Registry**
  - Increased longitudinal follow-up of NAFLD Registry for outcomes data
  - Post-marketing surveillance platform
- **Clinical Trial "Proving Ground"**
  - Response and/or pharmacodynamic biomarkers
  - Proof-of-principle for novel NIT-based trial designs
- **Data Analytics – Artificial Intelligence & Machine Learning**
  - Deep AI and Machine Learning analysis of extant EPoS/LITMUS dataset ('Omics', Registry/Phenotype-Outcomes, Histology)

Interested Industry Partners please contact: quentin.anstee@Newcastle.ac.uk

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EASL
European Association for the Study of the Liver
ASSISTANCE PUBLIQUE HÔPITAUX DE PARIS
UNIVERSITÄT BERN
UNIVERSITY OF HELSINKI
HÔPITAUX UNIVERSITAIRES PARIS NORD VAL DE SEINE
CIC bioGUNE
Biozientzietako Ikerkuntza Kooperatiboko Zentroa
Centro de Investigación Cooperativa en Biociencias
NOVARTIS
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TOWARDS BETTER MEDICINE
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IBBL
IFC CNR INSTITUTE OF CLINICAL PHYSIOLOGY NATIONAL RESEARCH COUNCIL
Exalenz Breathtaking Solutions
LITMUS

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www.litmus-project.eu

www.imi.europa.eu

HORIZON 2020

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efpia
European Federation of Pharmaceutical Industries and Associations

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