Berkeley School of Public Health

EASL European Association for the Study of the Liver

Forum for Collaborative HIV Research

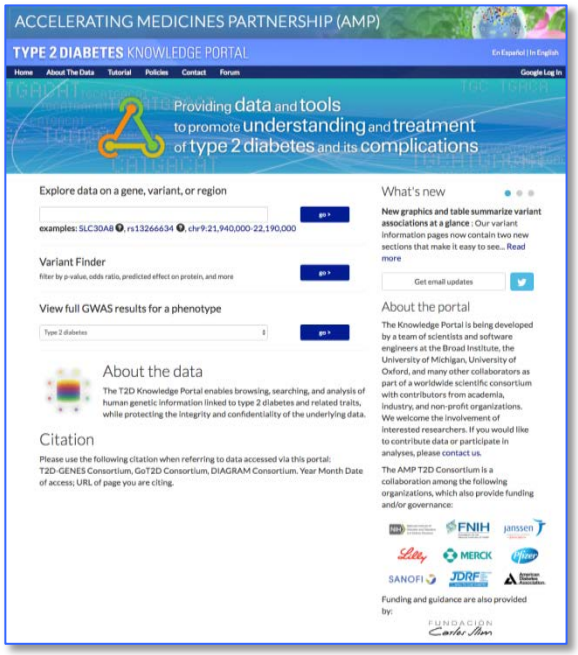
IMI: Accelerated Drug Portal

Julia Brosnan
on behalf of Innovative Medicines Initiative

Accelerating Medicines Partnership Type 2 Diabetes (AMP T2D)

AMP T2D is a pre-competitive partnership among government, industry, and nonprofit organizations.

The goal is to harness collective capabilities, scale and resources toward improving current efforts to develop new therapies for diabetes and its complications based on human genetics.

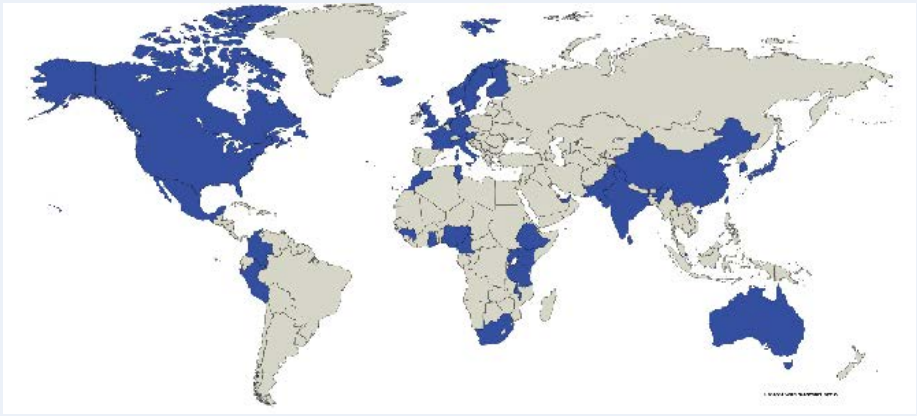


T2D Knowledge Portal
www.type2diabetesgenetics.org

Data in the Knowledge Portal today

- 17,000 T2D Exomes from T2D-GENES, SIGMA, GoT2D
- Exome chip results for ~82,000 samples of European ancestry
- Whole genome sequencing results from ~3,000 from GoT2D
- GWAS data for 9,000 samples of Mexican and Latin American ancestry
- GWAS results from 12,171 cases and 56,862 controls (gender-stratified, MetaboChip, and fine mapping results)*
- Meta-analysis results from GWAS Consortia: MAGIC, CARDIoGRAM, CKDGen, GIANT, GLGC (updated October 2016; 366,729 samples added overall)*
- 1000 Genomes
- ExAC integrated
- GWAS for 3,700 samples from (CAMP) Cardiology and Metabolic Patient Cohort*

Expanding our reach



4K Childhood T2D

25K

T2D Exomes

DIAGRAM

1000G

T2D-GENES

T2D

MAGIC

COHORTS FOR HEART AND AGING RESEARCH IN GENOMIC EPIDEMIOLOGY

NIH

FNIH

Next GWAS:
1,100,000 samples

Next exome chip:
820,000 samples

Next exome sequencing study:
55,000 samples

Open solicitations for New Data for the Portal

Three RFPs have been released by the FNIH. Funding awards will be made to proposals exhibiting the highest quality and that can demonstrate the greatest impact on the Knowledge Portal

T2D Related Complications:

- **Nonalcoholic Steatohepatitis (NASH)**
- **Nephropathy, with an emphasis on subjects with T2D**

T2D:

- **Enhancement of individual level and whole exome sequencing**

General requirements:

- Individual level genotype and deep phenotype data from existing data sets or newly generated data from readily available and properly consented samples
- Large cohorts or assembled data from multiple studies
- Longitudinal and familial studies will also be considered

Information on how to submit a proposal can be found at:

http://fnih.org/ampt2d

DEADLINE FOR SUBMITTING PROPOSALS: December 31, 2016

Identification and Validation of Non-invasive Biomarkers Across the Spectrum of Non-Alcoholic Fatty Liver Disease (NAFLD)

Julia Brosnan (Pfizer) on behalf of the Diabetes and Metabolic Disorders SGG

Pfizer, Lilly, BI, Novo Nordisk, Sanofi, Novartis, Ellegaard, Somalogic

innovative medicines initiative

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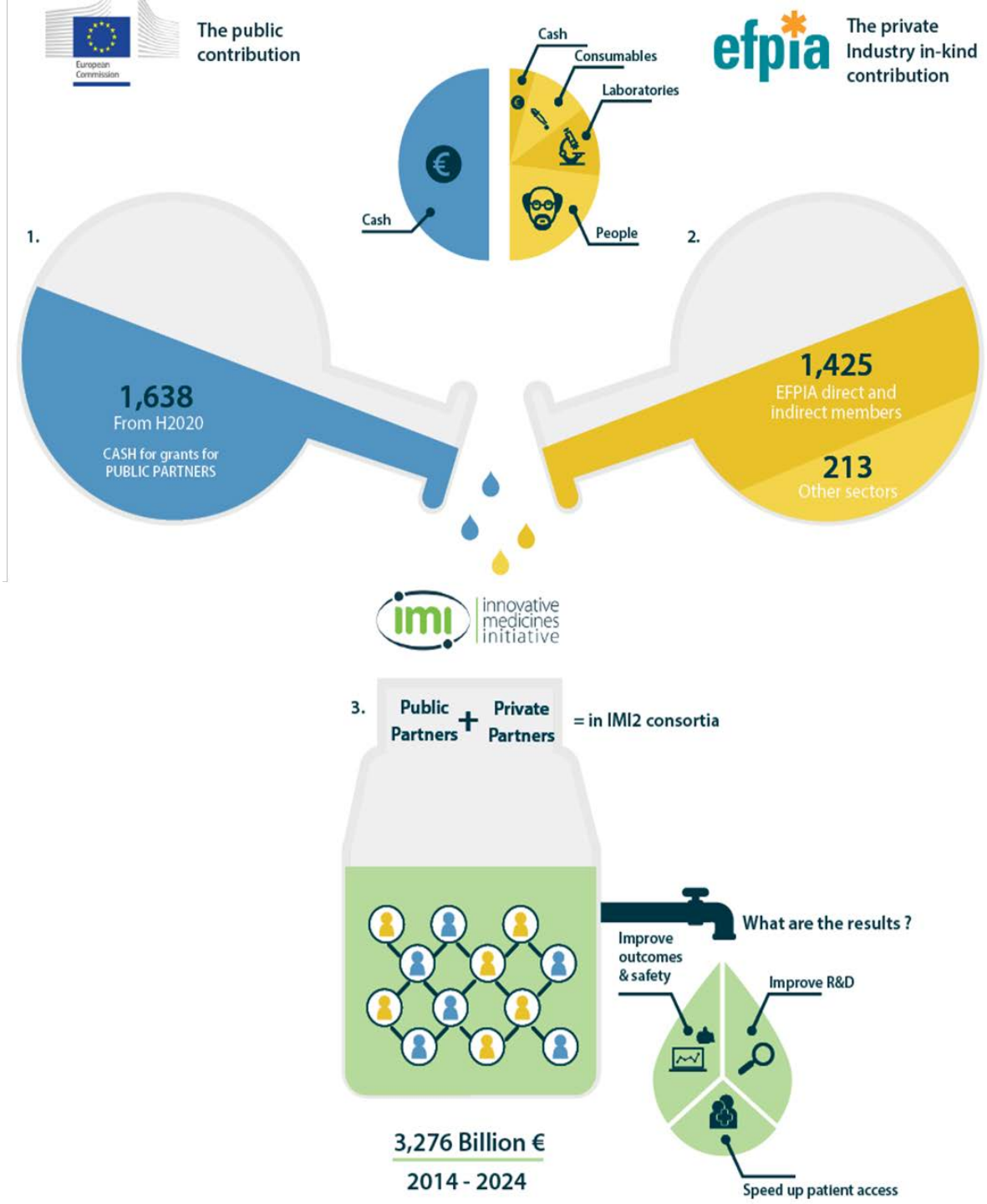
Diabetes / Metabolic Disorders



Focus on unmet needs

Non-competitive collaborative research

Competitive Calls for proposals

Pooling expertise, knowledge and resources, cross-fertilisation

Developing incentives to address major unmet medical needs

Providing a neutral trusted platform to align public and private interests

Central Challenge

Critical need to establish non-invasive biomarkers for diagnosing and classifying subjects within the NAFLD spectrum, and in particular identifying those with NASH and predicting those likely to progress to NASH.

Identifying and validating biomarkers that can be employed to track disease progression, as well as response to intervention is crucial in furthering advances in clinical care and drug development for NASH and will enable clearer understanding of the heterogeneous outcomes of NAFLD.

Clear consensus that a lack of diagnostic, prognostic and treatment response NASH biomarkers hampers clinical practice and seriously impedes drug development.

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Why the need for public-private collaborative research?

Candidate Biomarkers

- Relatively small studies.
- Rarely been replicated.
- None been validated against liver biopsies
- Need to be studied systematically
- Sufficiently powered investigation.
- collation of relevant existing clinical research
- best addressed by a comprehensive public-private collaboration.

Liver Biopsy

- Currently the basis for diagnosis and staging of severity of NASH.
- Basis for adjudicating effectiveness of intervention
- On-treatment liver biopsy required for registration of novel treatment.

Validating non-invasive biomarkers against liver biopsy in an appropriately designed, sufficiently powered study is needed to bridge the contemporary standards for clinical practice and drug development.

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What's the purpose of this IMI2 initiative?

Bring together a level of funding and multi-stakeholder commitment sufficient to definitively address biomarker challenges in NAFLD and NASH.

Avail existing NAFLD and NASH research cohorts and access samples that meet carefully considered criteria, importantly including properly adjudicated liver biopsy samples.

Employ standardized laboratory analyses, together with bioinformatics, to harmonize biomarker data, as well as accompanying clinical and liver imaging data.

Transformative for the field - needed to gain consensus acceptance by NAFLD basic and clinical investigators, instill confidence in the use of biomarkers for decision making by drug developers and ultimately, lead to regulatory approval of these biomarkers

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Proposed Stages

Validation of a Priori Hypotheses (Stage 1a)

- Identification of top markers from existing data
- Qualify by pooling available datasets
- Conduct standardized assays as needed
- Common data repository

Confirm and Complement (Stage 1b)

- Establish a prospective Global NAFLD Cohort (GNC) across the full spectrum of disease (detailed phenotyping, histology, biomarkers specimens, imaging).
- Expected to extend existing studies
- Confirm the identified top candidates in the GNC

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What Will the Applicant Consortium Look Like?

- Led by scientists/physicians who are recognized experts in liver disease and specifically in NAFLD and NASH
- Encompass subjects with the full spectrum of NAFLD (informed consent).
- Cohorts should be longitudinal research efforts with high quality follow-up procedures together with a high level of participant retention.
- Liver biopsy and clinical data must be available
- Enriched with later stages to support NASH biomarker qualification.
- Data that exclude causes of liver disease other than NAFLD and NASH.
- Cohort size estimated to be a minimum of 1,500 to 2,500 subjects

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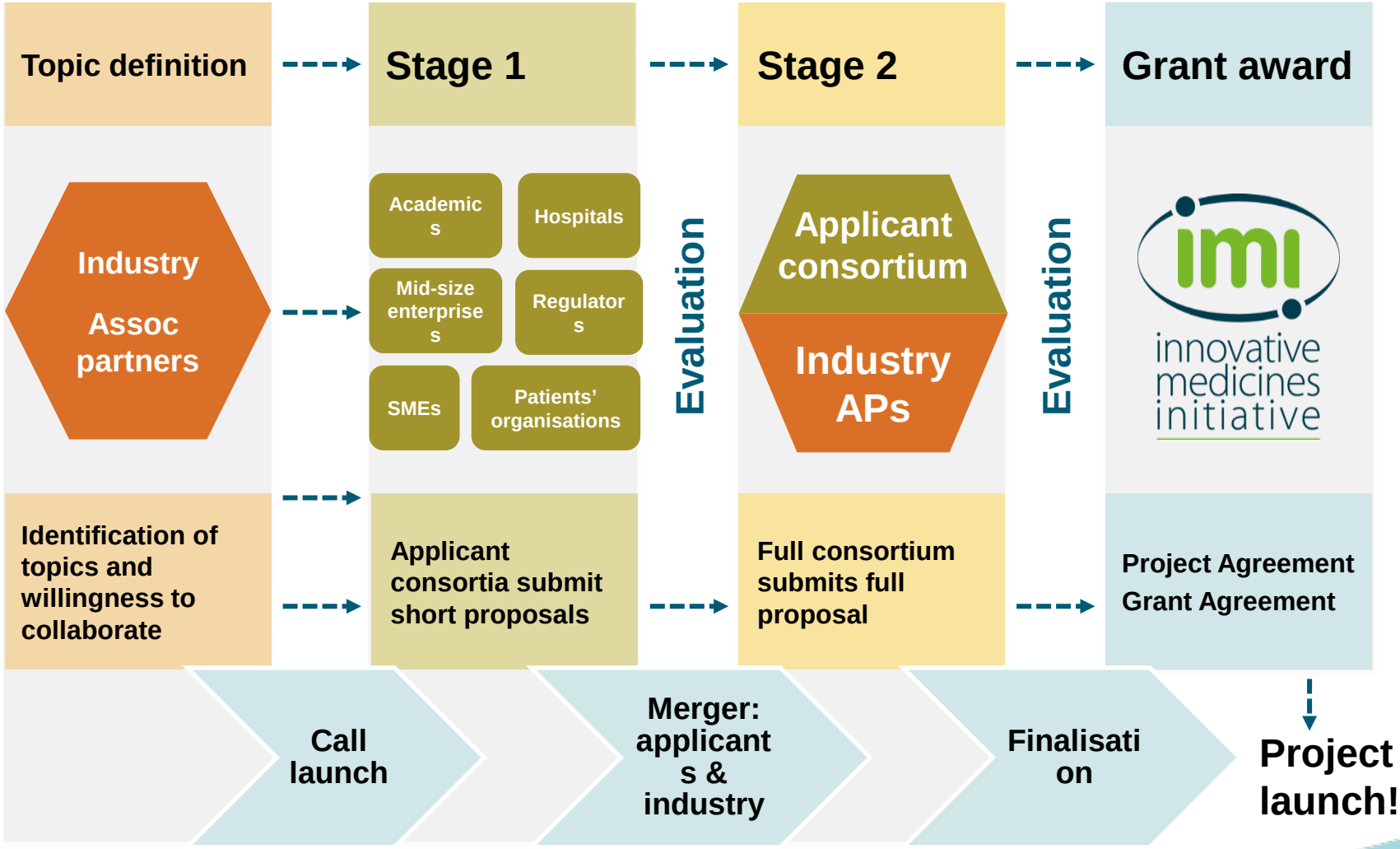
Expected Deliverables

1. Baseline characteristics/biomarkers of patients with NAFLD that can diagnose NASH and predict better disease progression across the spectrum of NAFLD;

2. Validation of non-invasive biomarkers for stratification of subjects (e.g. fast progressors) for clinical trial inclusion and

3. The identification of candidate biomarkers that can serve as surrogate markers for clinical outcomes of NASH

Typical IMI 2 Stages Call process



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