



EUROPEAN LEAD FACTORY

Game changing for innovative medicine

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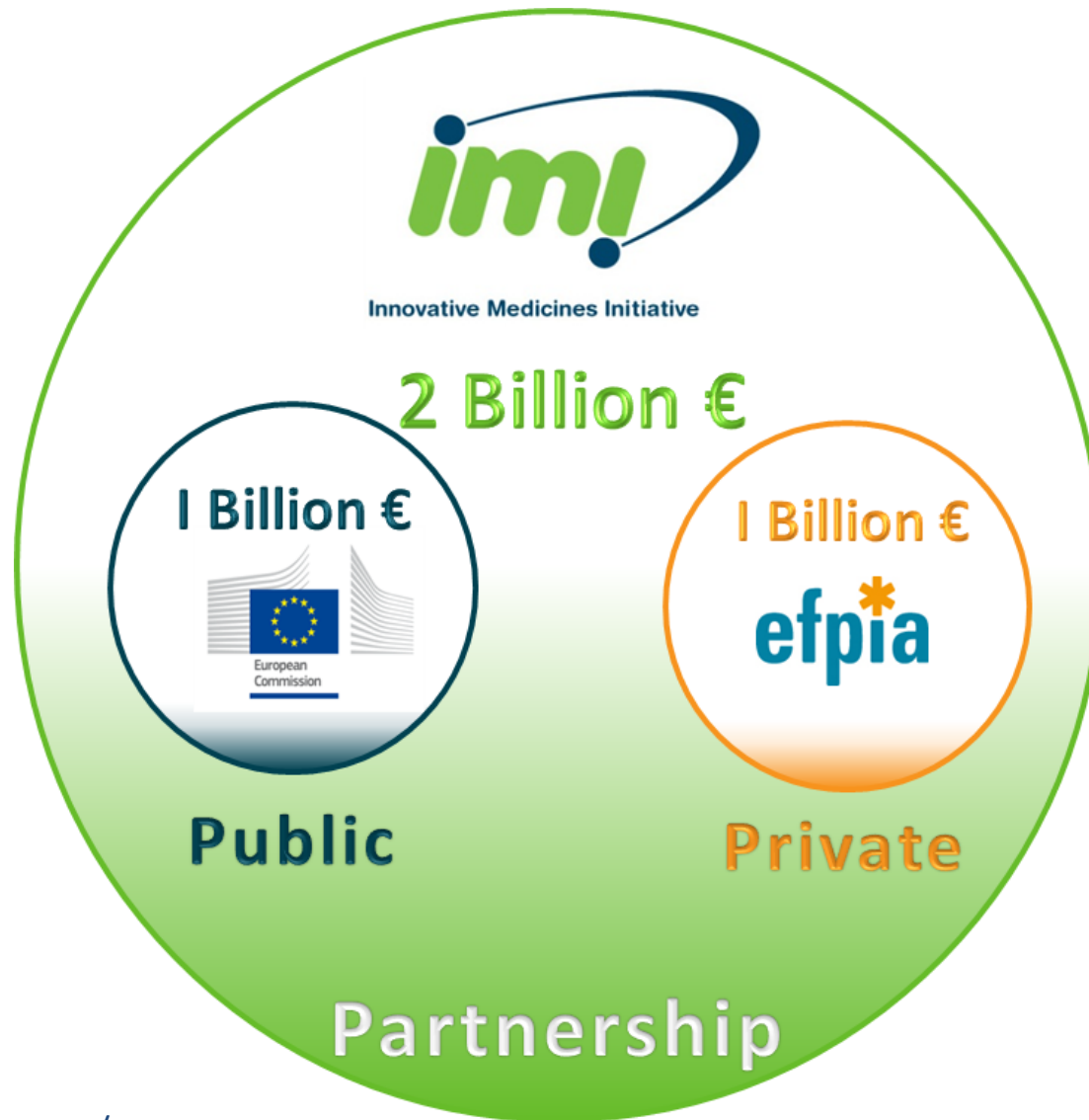
Dear reader,

Only the official and formally signed contractual documents in relation to the EU Lead Factory (the Project Agreement, Grant Agreement, the Description of Work, and Third Party Access Agreements) have a binding value in relation to the subject matter covered in these slides.

Any information contained in these slides is not binding upon the parties and can in no event be used to interpret or complement the formally signed contractual documents referred to above.

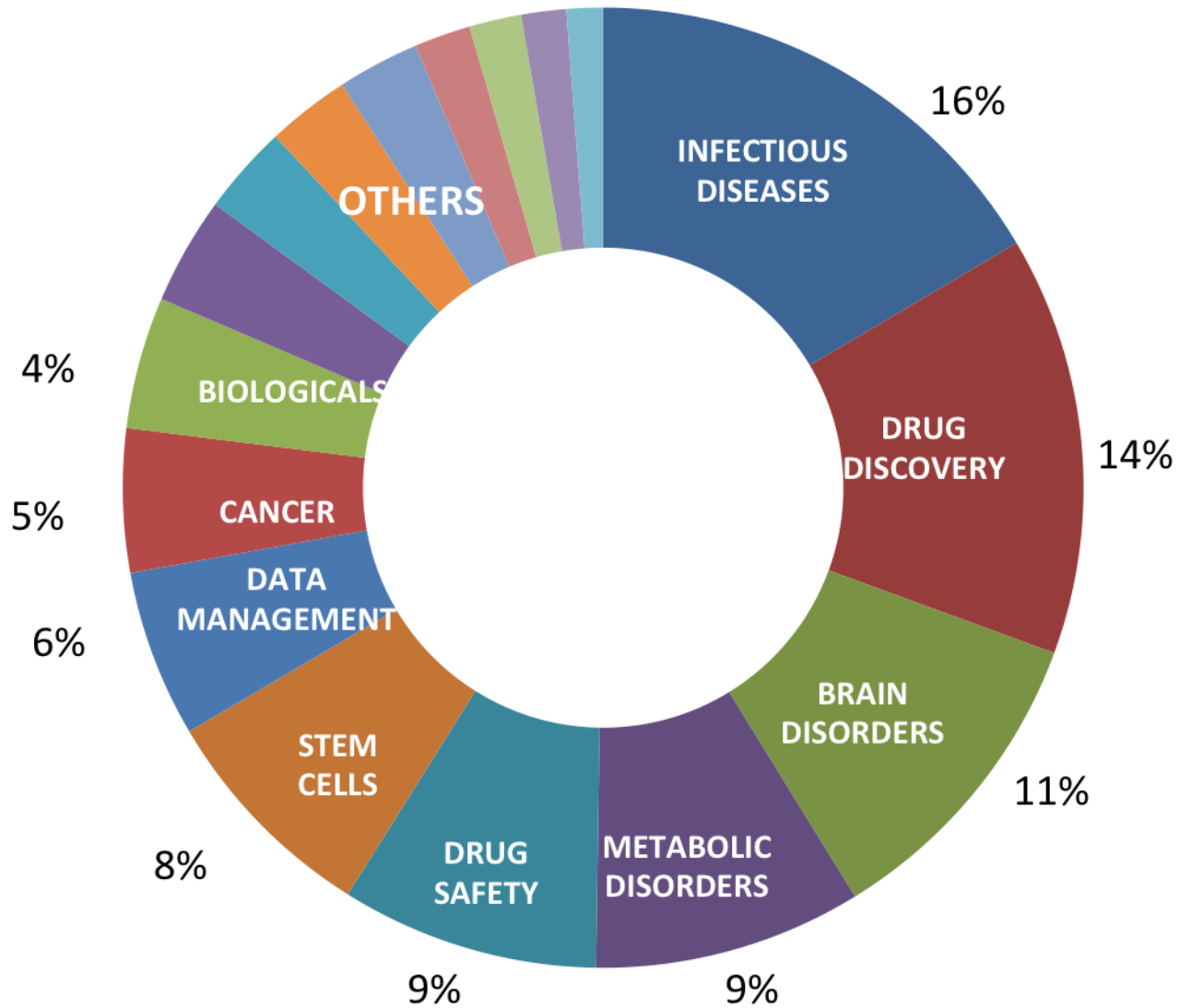
The EU Lead Factory Team

Innovative Medicines Initiative

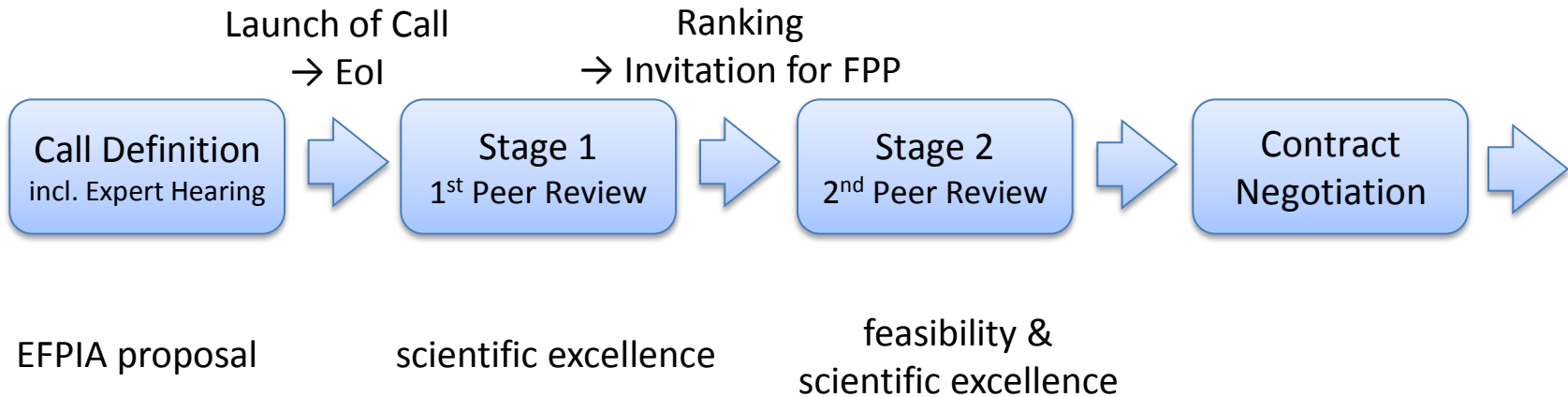


<http://www.imi.europa.eu/>

IMI portfolio – budget breakdown



IMI Consortium formed through a Multi-Step Process



- ➔ rigorous expert review at multiple steps
- ➔ selection of public partners *via* independent expert panel
- ➔ IMI Grant Agreement sets general framework for Intellectual Property Regulations
- ➔ IMI supervision ensures highest ethical standards and fair treatment of all partners

The IMI Family



Use the IMI funding to become:

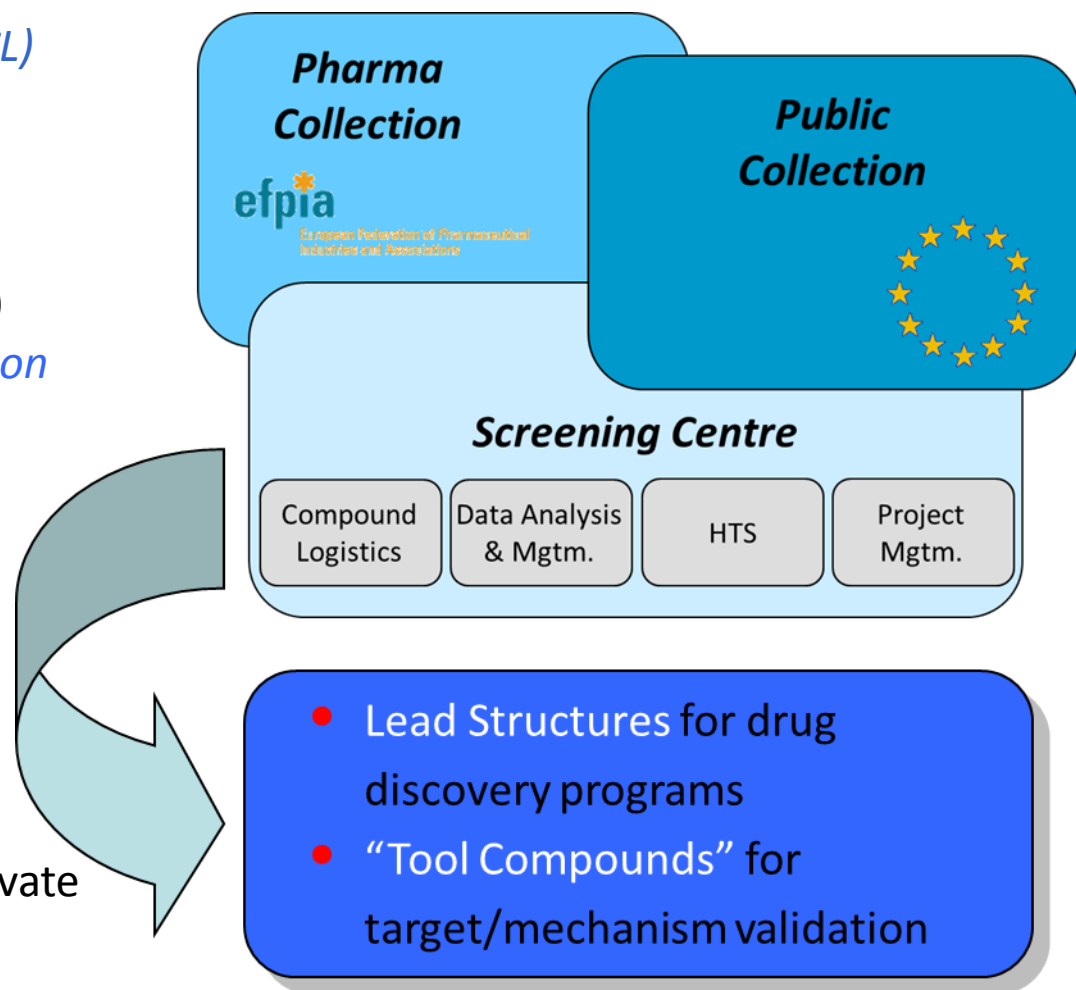
- The Open Innovation model of choice for Lead Discovery for EFPIA members
- A flagship facility for IMI / EU with a world class cluster of discovery businesses around it
- The preferred partner for Lead Discovery for public partners (Academia, Patient Organizations, NGOs etc.)

AND

Maintain and further enhance that position
after the IMI funding period

Architecture of the EUROPEAN LEAD FACTORY

- ❑ building a comprehensive *Joint European Compound Library (JECL)* accessible for private and public lead discovery programmes
- ❑ JECL is comprised of a *Pharma Consortium Collection* (≥ 300.000 compounds) and a *Public Collection* (up to 200.000 cpds.) generated in the context of this project
- ❑ the *Screening Centre* takes responsibility for cpd. logistics, HTS, data analysis & handling, and programme mgmt.
- ❑ Screening Centre functions as a market place to broker public-private discovery programmes with the Pharma Consortium



The Objectives

Strong output of innovative leads through:

- Unique & top quality compound library composition
- Highly innovative screening programmes
- Professional project execution

Consortium excellence through:

- In depth scientific interaction with all partners
- Honest brokerage (IP, Publications etc)
- Communication and Education

Consortium with 30 Public and Private Partners

150 employees combining **agility** of SME's, **experience** of Pharma and **innovation** of Academia

AstraZeneca

SANOFI

BAYER

janssen
PHARMACEUTICAL COMPANIES
OF Johnson & Johnson

Lundbeck

MERCK

EFPIA

Public Compound Collection

The University of Nottingham

VUmc
VU University
Medical Center
Amsterdam

GAB:mi

UNIVERSITY OF LEEDS

Radboud Universiteit Nijmegen

MAX-PLANCK-GESELLSCHAFT

Universiteit Leiden

NKI-AVL

university of groningen

UNIVERSITÄT DUISBURG ESSEN

DTU

UNIVERSITY OF OXFORD

BIOCITY SCOTLAND

pivot park

UNIVERSITY OF DUNDEE

TPharma

European Screening Centre

Lead Discovery Center
LDC

ChemAxon

SYNCOM

SYGNATURE
discovery

MERCACHEM

TAROS
Chemicals

EDELRIIS
MEDICINAL KEYMISTRY

Chemistry SMEs

EU Lead Factory invites Public Contributors

- fusion of 2 largely independent consortia:
Screening Centre and Chemistry (Compound Collection)



- not a ‚closed-shop‘ setup:
„Contributing Third Parties“ from
Public Domain – *Target Programme
and Library Proposals*

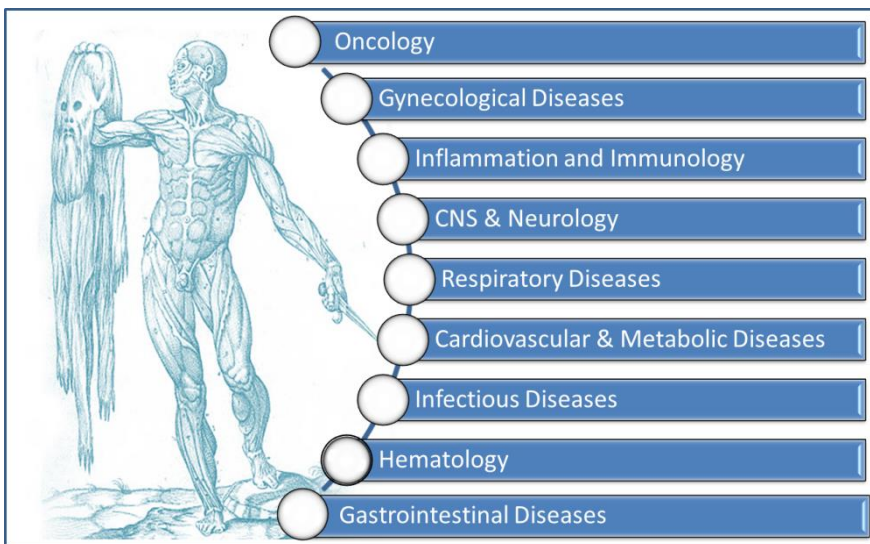
- handling of confidential information and know-how from Participants
 - covers also competitive research aspects and aims for value generation
- strives for sustainability

Target Owners: EU Lead Factory invites Public Contributors

What are we looking for:

- *novelty (target or assay approach)*
- *highest scientific quality*
- *molecular target programmes only*
- *HTS compatible assay available*

- *within indication spectrum of EFPIA partners*



... or beyond!

Target Proposal

Programme Office

- TI Pharma -

- Eligibility
- Differentiation from Past Selected Prgms.
- Differentiation from EFPIA

Screening Review Board

Head PO, CSO PPSC, CSO Dundee + 2 EFPIA

- (Assay) Technical Assessment Dialogue

Screening Selection Committee

Head PO, CSO PPSC, CSO Dundee + 7 EFPIA + 4 Ext. Advisors

- Quality of Science • Novelty • Portfolio Balance

Target Programme

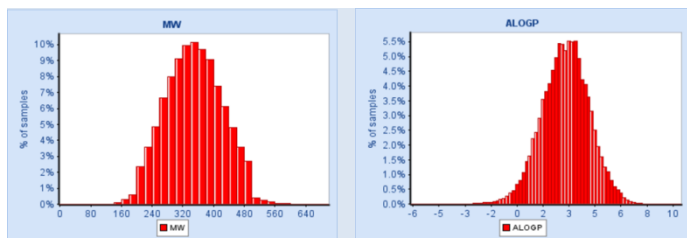
Target Owners: The Consortium Offer

- Unique, high quality library with 2 sets of compounds:
 - 300.000 EFPIA compounds not commercially available
 - 200.000 innovative compounds from chemistry consortium
- State of the art compound logistics and screening facilities
 - Compound logistics and hit picking at Biocity Scotland
 - uHTS screening at Pivot Park Screening Centre in The Netherlands
- Assay Development
 - Protein production, functional testing and crystallography at Oxford University
 - HTS conversion of existing assays at Pivot Park Screening Centre
- Hit follow-up and Cheminformatics
 - Hit characterization and initial SAR development at University of Dundee

Target Owners: EFPIA Library Characteristics (1)

Quantitative Estimate of Drug-Likeness (QED)

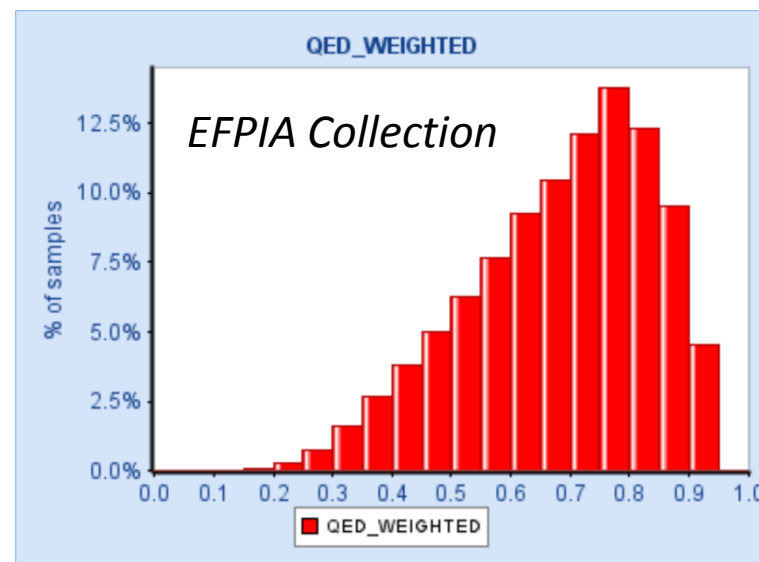
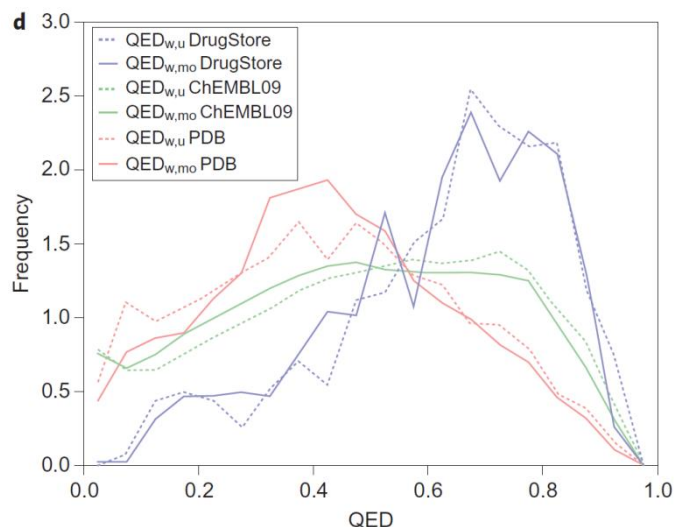
Bickerton *et al.*,
Nature Chemistry 4 (2012), 90-98



- MW
- octanol–water partition coefficient (ALOGP)
- # hydrogen bond donors (HBDs)
- # hydrogen bond acceptors (HBAs)
- molecular polar surface area (PSA)
- # rotatable bonds (ROTBs)
- # aromatic rings (AROMs)
- # structural alerts (ALERTS)

$$\text{QED}_w = \exp\left(\frac{\sum_{i=1}^n w_i \ln d_i}{\sum_{i=1}^n w_i}\right)$$

*Weighted Composit of Desirability Functions (d)
derived from Drug Reference Set (ChEMBL Drug Store)*

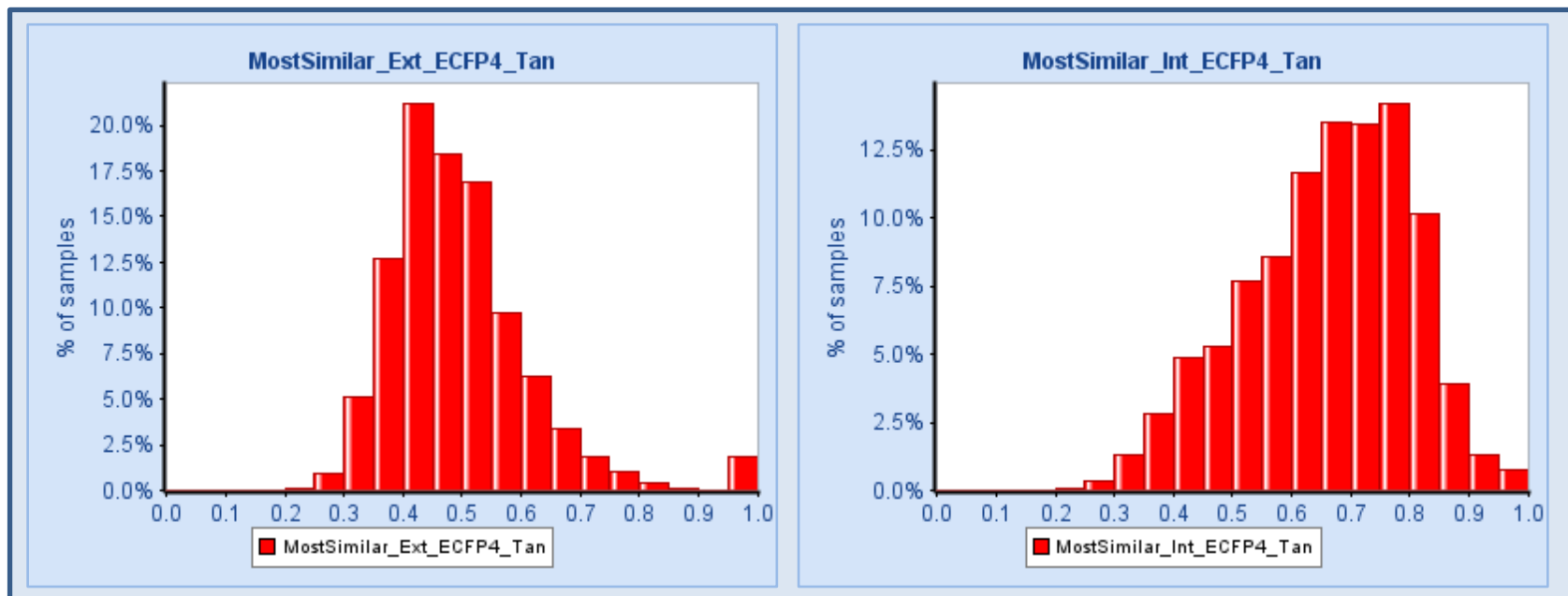


→ EFPIA Collection ideally reflects current view on Drug-Likeness

data kindly provided from Prof. Andrew Hopkins, University of Dundee

Target Owners: EFPIA Library Characteristics (2)

Structural Diversity in Pharma Consortium Collection



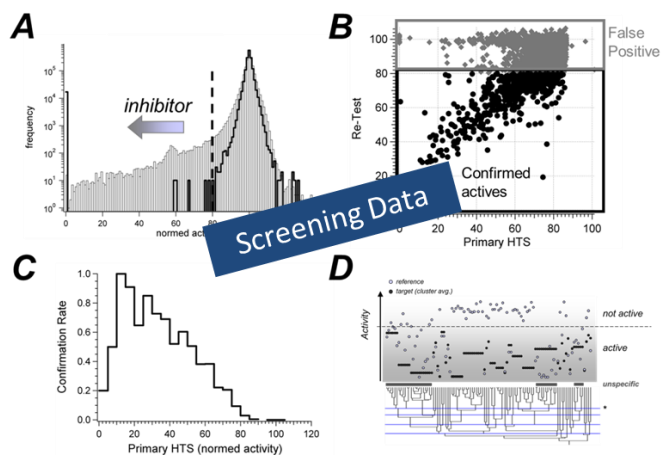
Ext = 1 company vs all the others (most similar compound from the other sets)

Int = 1 company vs itself (most similar compound within the same set)

→ Complementary EFPIA subsets add to uniqueness and quality of the European Compound Collection

data kindly provided from Prof. Andrew Hopkins, University of Dundee

Target Owners: The 'Qualified Hit List' is Main Deliverable



QHL/IHL Data

Structure	Identifier	Cpd. Owner	Assay 1	Assay 2
	ELF 001785	SME1 Part. 07	0.5E-06	>20E-06
	ELF 031586	SME1 Part. 11	3.0E-06	>20E-06
	ELF 789116	SME4 Part. 01	0.3E-06	>20E-06
	ELF 000346	EFPIA 01	1.3E-06	>20E-06
	ELF 243561	EFPIA 03	1.1E-06	>20E-06

- limit information drain from proprietary compound collection to only **relevant results**
- assay statistics and screening data w/o explicit chemical structure information
- list per Target Programme containing **up to 50 chem. structures** of compounds
- cleared by Compound Owner
- Programme Owner has sole discretion to decide on future exploitation of QHL results
- Programme Owner will be granted
 - Access Rights for Direct Exploitation
 - 3-year exclusivity period

Target Owners: The Partnership Case

Target Programme Owner's...

Rights

Exploitation of unique
Compound Library and
Screening Facility

Access Rights and 3 Year
Exclusivity to Exploit
Qualified Hit List Results

Control of Target
Programme Progression:
Research or Direct Exploitation

Obligations

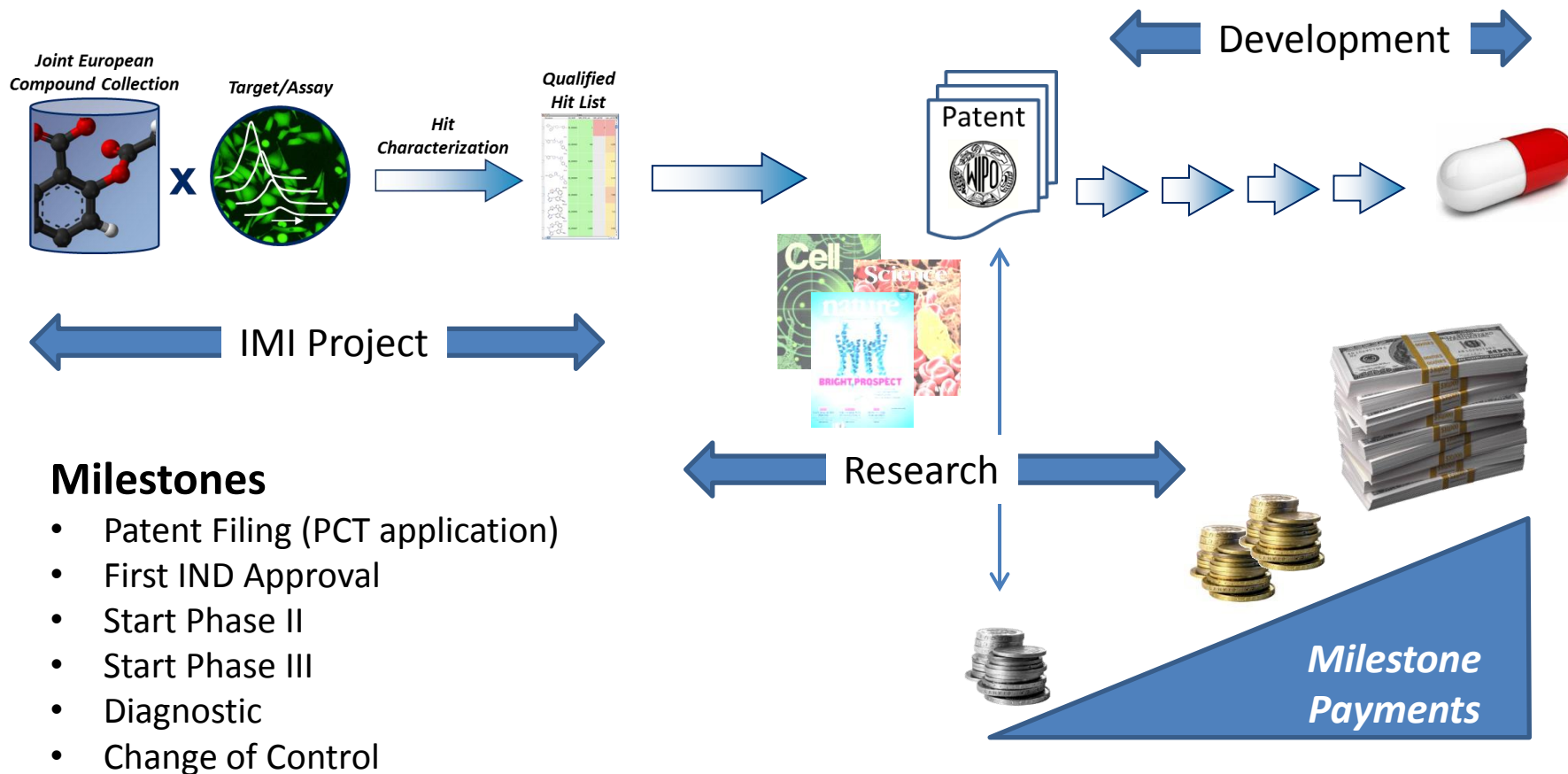
**Access Rights and
Dissemination**
(IMI's IP Policy)

Compensation
to EU Lead Factory
- for Direct Exploitation only -

Option for EFPIA
to license Target Programme for
Direct Exploitation

Target Owners: The Partnership Case

Financial Compensations, i.e Milestone Payments, to EU Lead Factory Consortium (EUC²LID) for Direct Exploitation only



Target Owners: EFPIA Partnership Option

- Programme Owner grants to EFPIA Participants the right to submit first bid for Direct Exploitation
- at any time during the 3-year exclusivity period
- obligatory step preceeding publication or partnering to Third Party
- balances EFPIA's investments and partnering interests
- ensures value generation from EU Lead Factory results
- provides Programme Owners with access to potential partners for Direct Exploitation



Target Owners: Dissemination & Publication Approval

Publication Approval Committee

Proposed publication in relation to Foreground owned by proposing Participant

Instruct author to delay, or rewrite & resubmit



submit 45 days before planned dissemination



1 EFPIA Representative (or Delegate)
Head of EU Screening Centre (TI Pharma)
Head of Chemistry (Taros)
1 Academic Member of IP Committee

15 day review period (protection value generation)

Circulation to all Participants

30 day Objection Period

unanimous objection

No unanimous objection

1. Protection of objecting Participants FOREGROUND: 90 d
2. Removal of Confidential Information: *asap*
3. Interest in subject matter : 180 d
negotiate license/collaboration agreement



Publication

when all Objections addressed

Target Owners: The European Lead Factory invites ...



... public institutions and small/medium enterprises to submit innovative target programme proposals aiming at the discovery of small molecule hits for drug development or research.

Please submit at

targetproposals@europeanleadfactory.eu

Chemistry: Partnership Case

A Unique Opportunity for Translating Early Ideas into novel Chemical Libraries for screening

Compensation

- fixed Monetary Rewards -

Ownership

- ownership retained on idea -

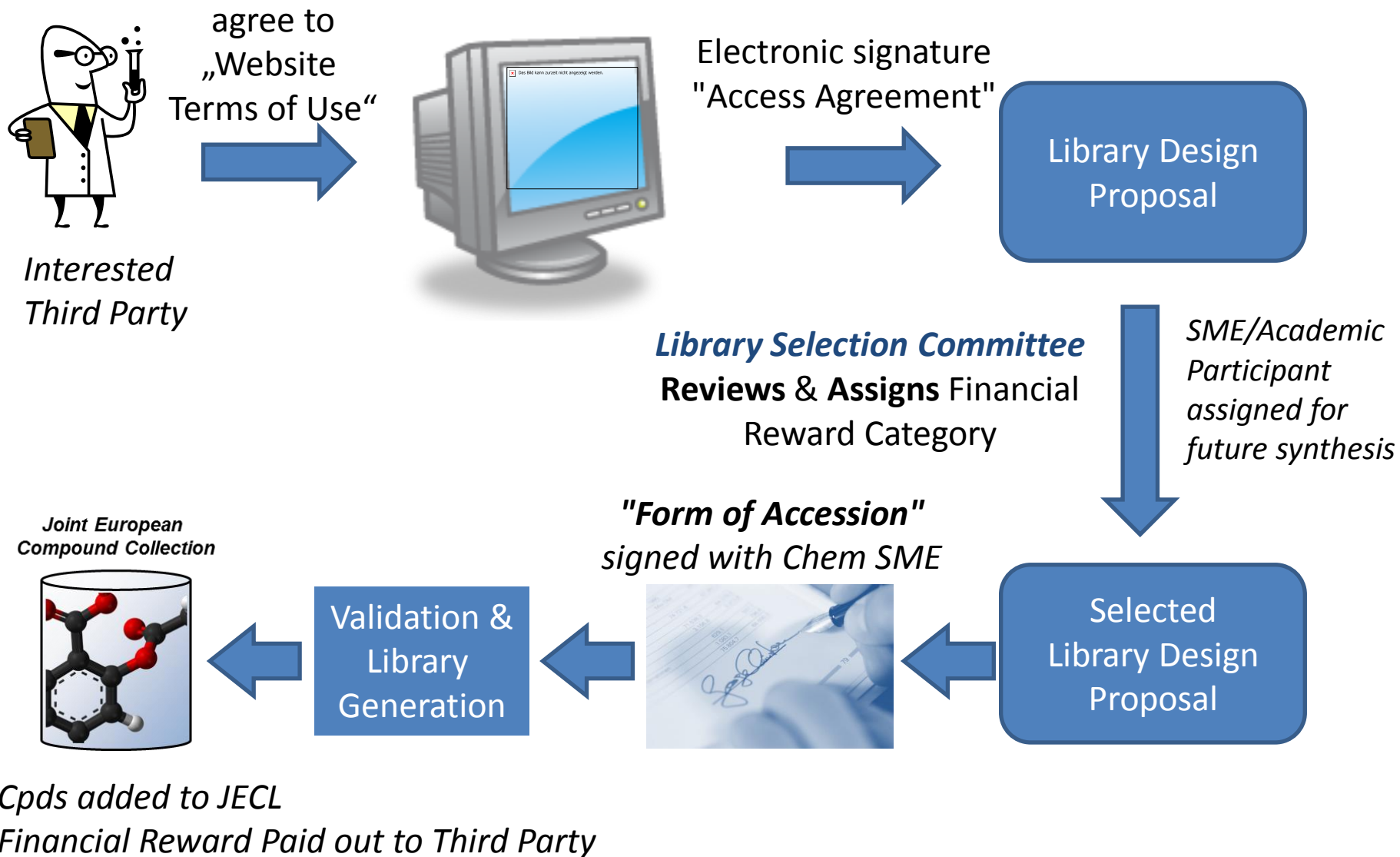
Access Rights to Consortium Participants

- Exclusive & Royalty Free -

Chemistry: Criteria for the Review of Library Proposals

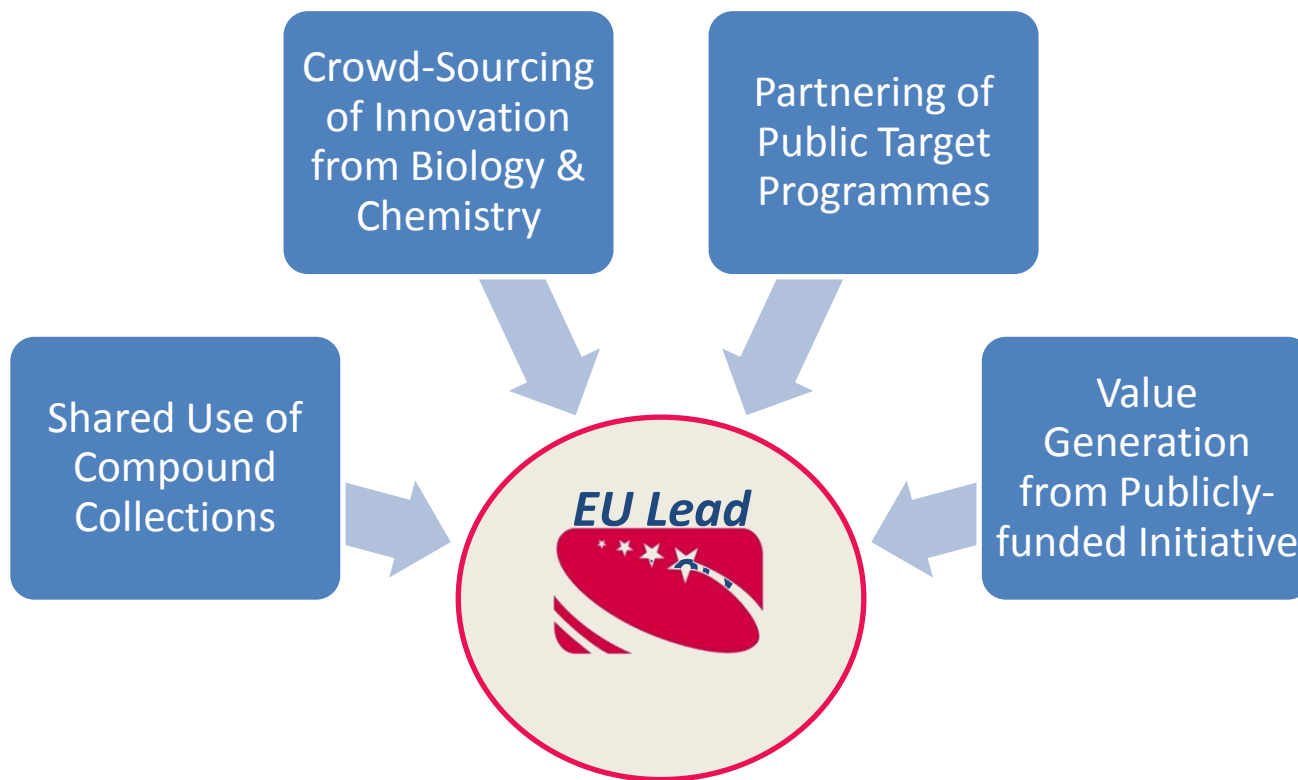
- Proposals are scored against six criteria
 - Molecular properties
(scored for drug-likeness with preferred $\text{clogP} < 4$)
 - Structural features
 - Novelty
 - Diversity potential
(ideally, proposals can yield >500 final compounds)
 - Synthetic tractability
 - Innovation

Chemistry: Crowd Sourcing of Library Design Proposals



The European Lead Factory

... a large-scale controlled experiment:





EUROPEAN LEAD FACTORY

Game changing for innovative medicine



The research leading to these results has received support from the Innovative Medicines Initiative Joint Undertaking under **grant agreement n° 115489**, resources of which are composed of financial contribution from the European Union's Seventh Framework Programme (FP7/2007-2013) and *EFPIA companies' in kind contribution.*