



European Lead Factory

Changing the Game for Innovative Medicine

Dr. Jon de Vlieger, Call Director

Madrid, 22nd June 2015

Dear Reader,

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

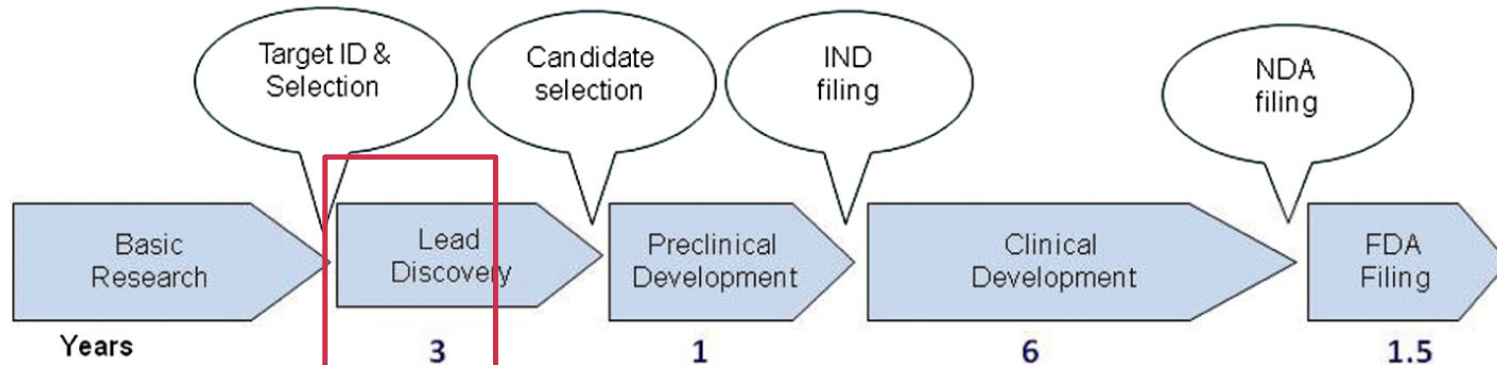
Any information contained in these slides is not binding upon the parties and can in no event be used to interpret or complement the formally signed contractual documents referred to above.



The European Lead Factory Team

Drug Discovery Process and ELF objective

JP Hughes et al. *Br J Pharmacol* **2011**, 162(6): 1239–1249.



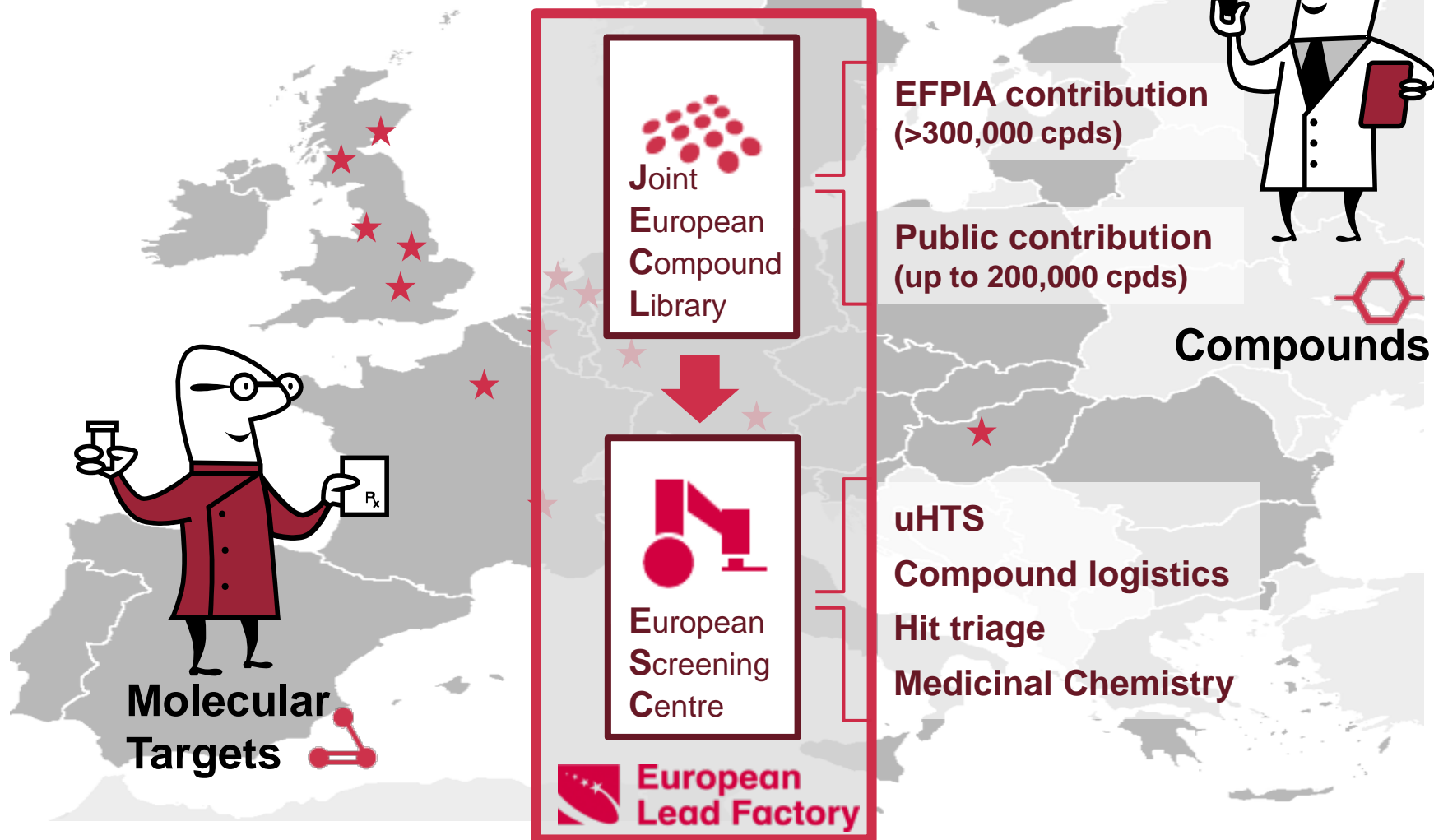
**Molecular
Targets** 

 **European
Lead Factory**

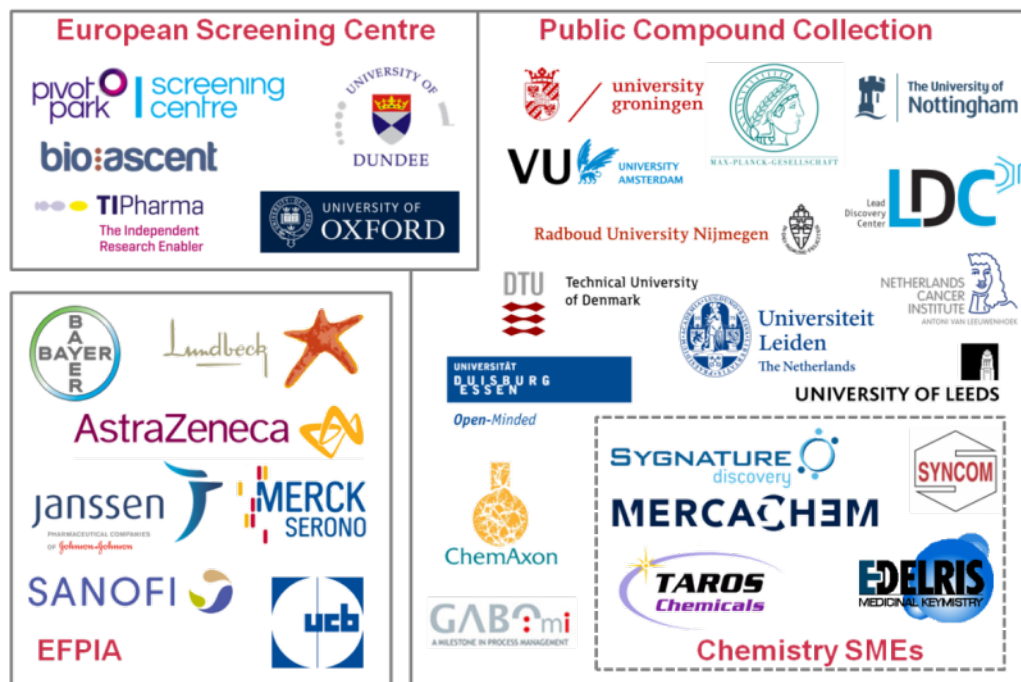


**List of qualified
hits (QHL)**

Collaborative Drug Discovery



Made possible by...

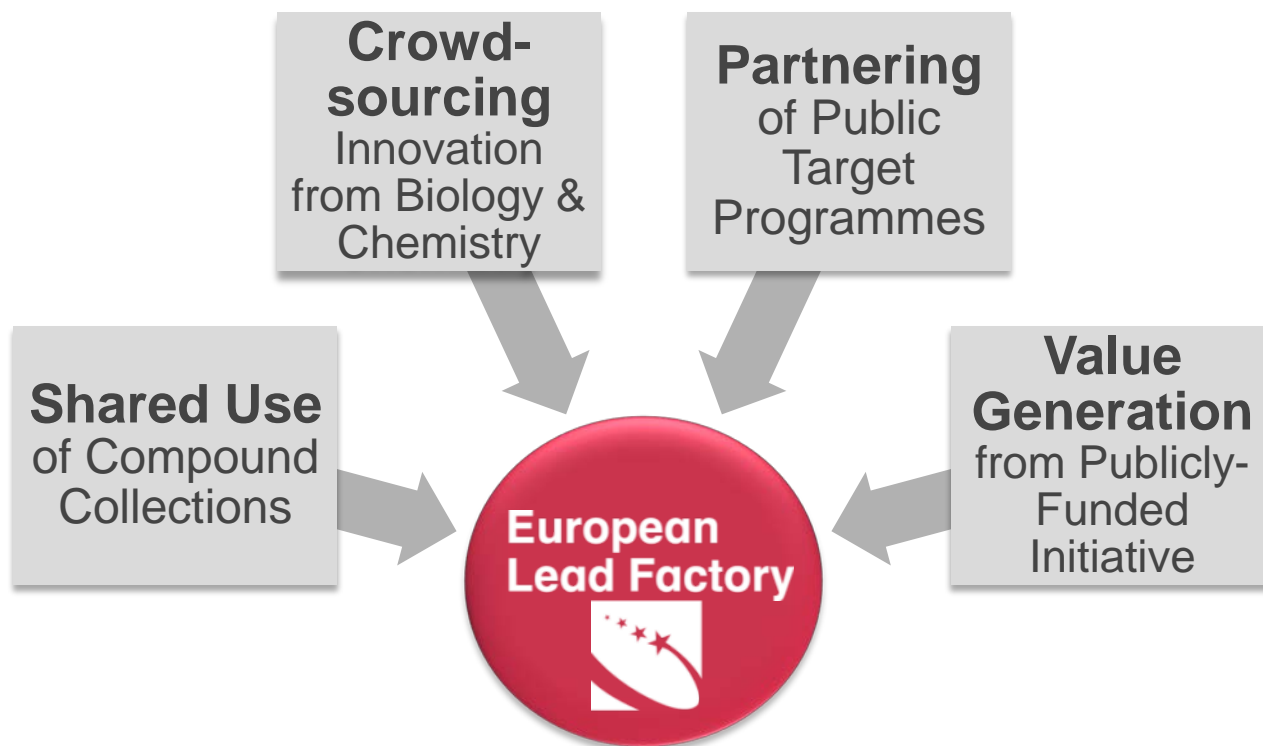


EU Lead Factory

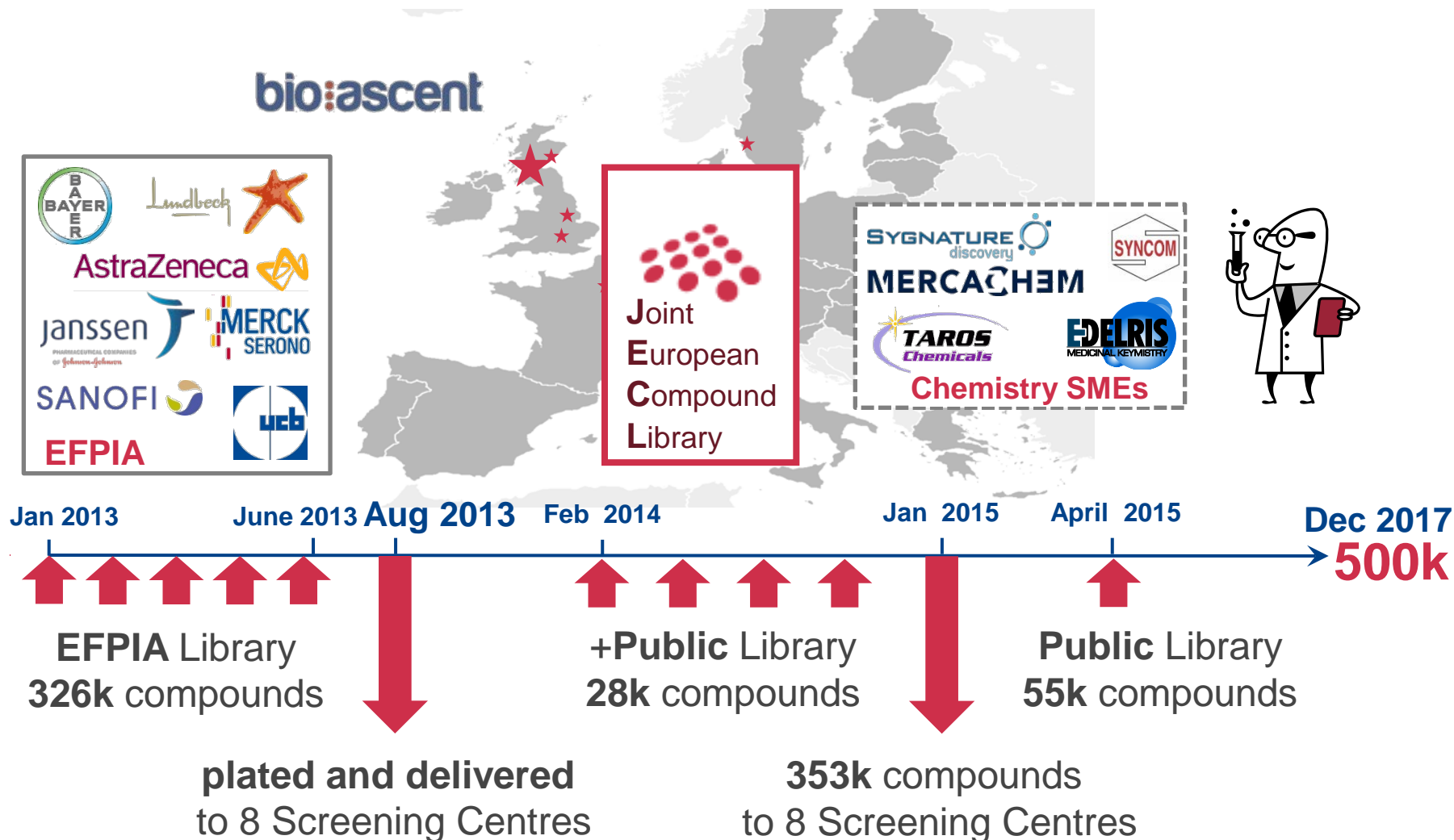
combines
innovation of Academia,
agility of SMEs,
experience of Pharma
and funding from



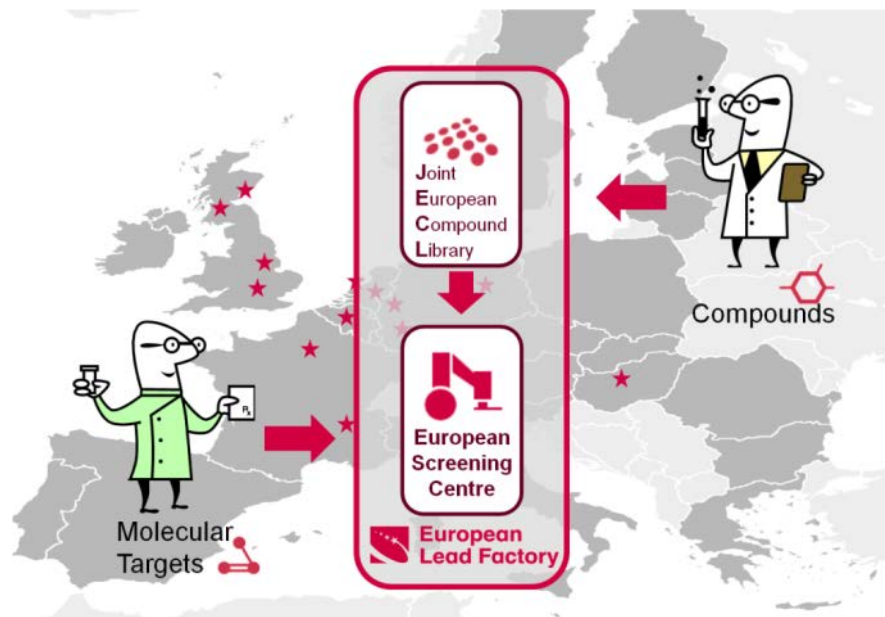
A Large-Scale Controlled Experiment




Building the JECL



Join us!



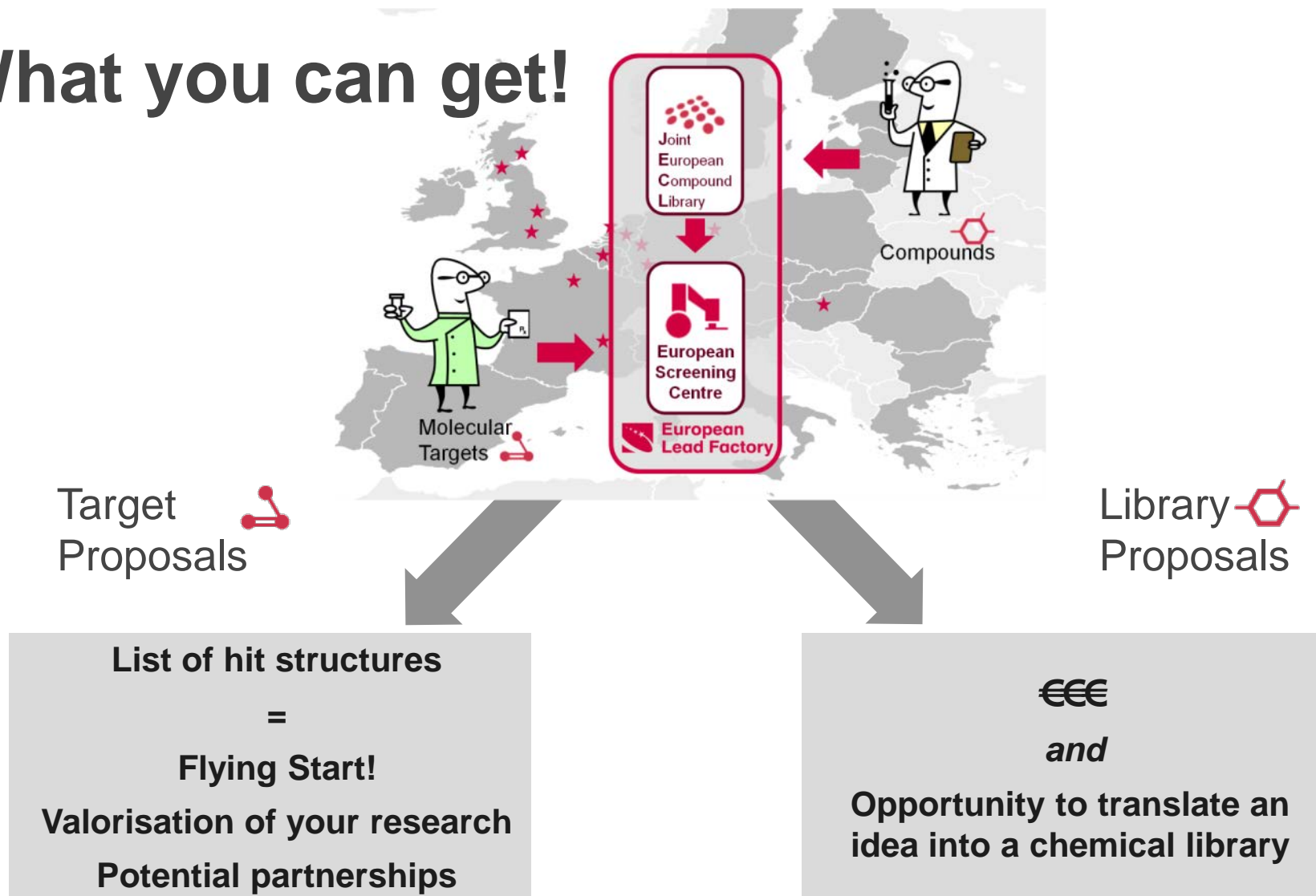
Target
Proposals 

Library 
Proposals

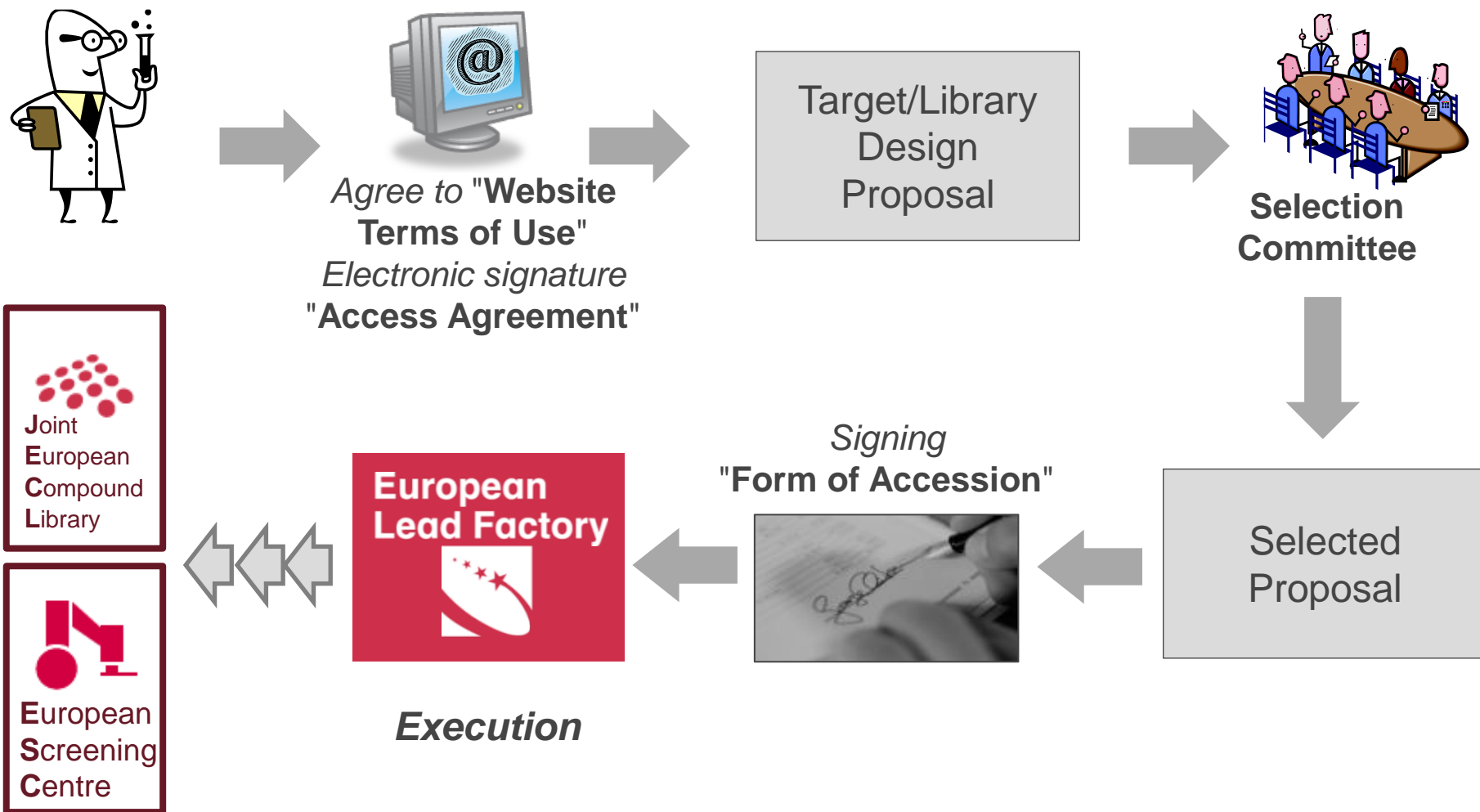
- Novelty (target or assay approach)
- Top scientific quality
- Defined molecular target
- HTS compatible assay

- Novelty
- Drug-like
- Diversity potential
- Synthetic tractability
- Innovation

What you can get!



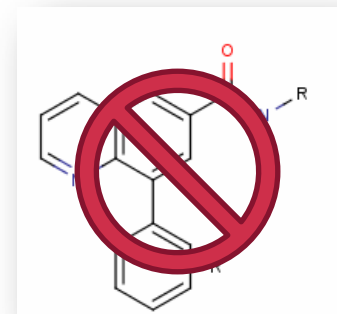
Accession process





Crowdsourcing Chemical Scaffolds

Library Proposal Criteria



Innovative library design

Novelty

Structural features

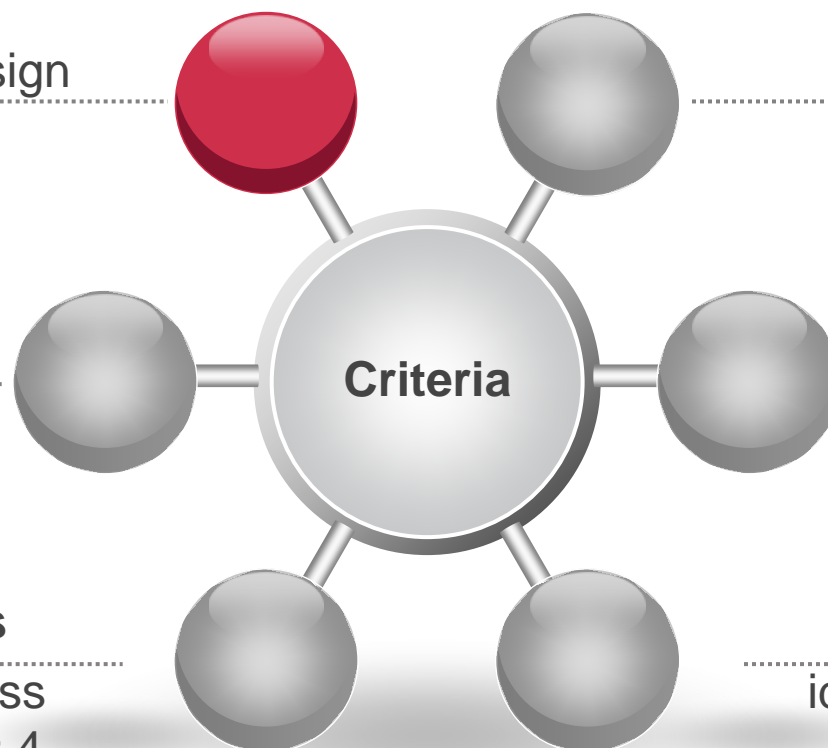
Synthetic tractability

Molecular properties

scored for drug-likeness
with preferred $\text{clogP} < 4$

Diversity potential

ideally, potential to yield
>500 final compounds

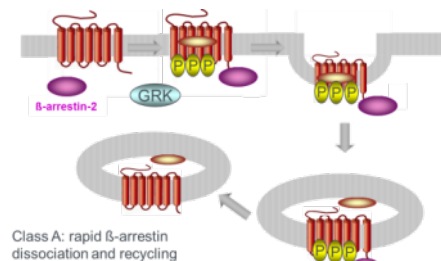


*European Lead Factory currently strongly prioritizes **fully validated** library proposals*

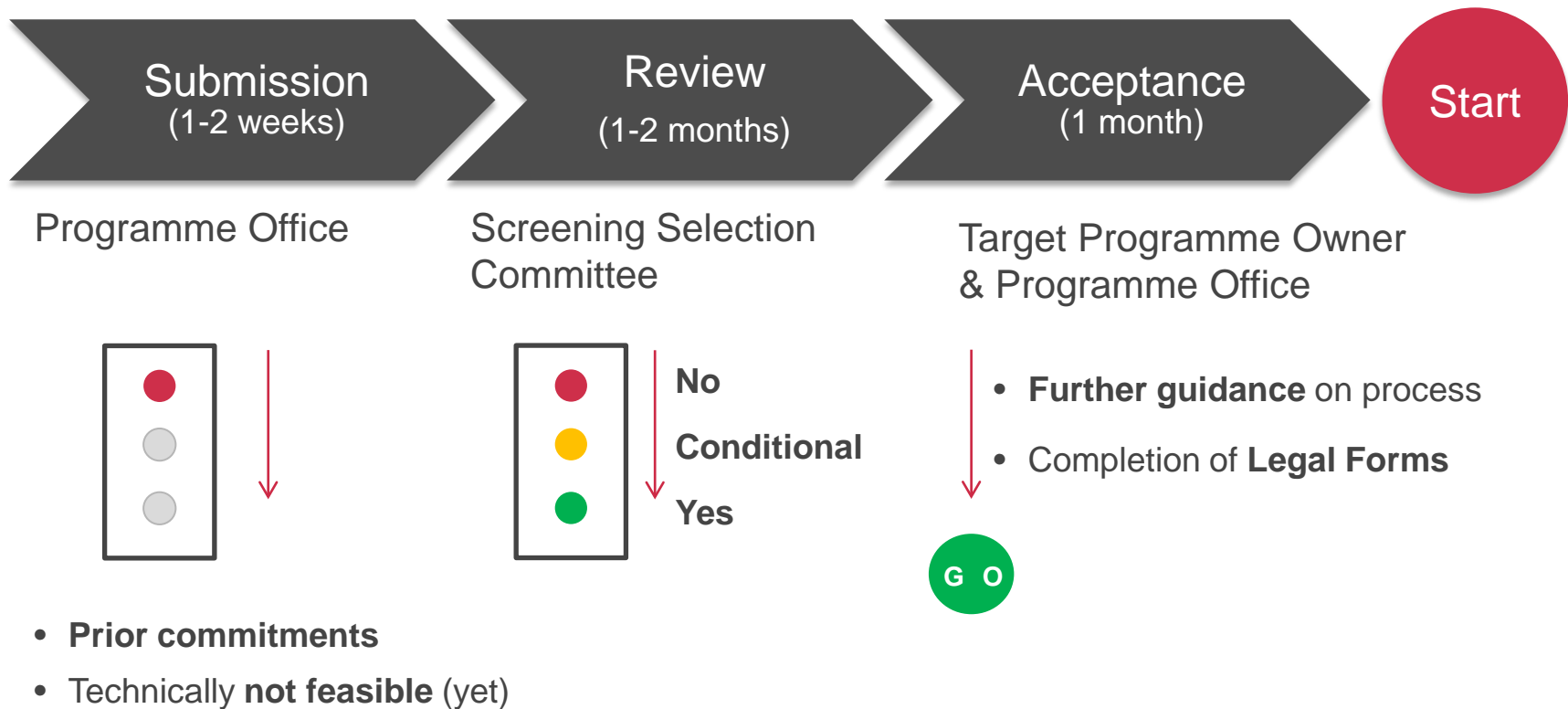
Crowdsourcing Biological Targets

Target Proposal Criteria

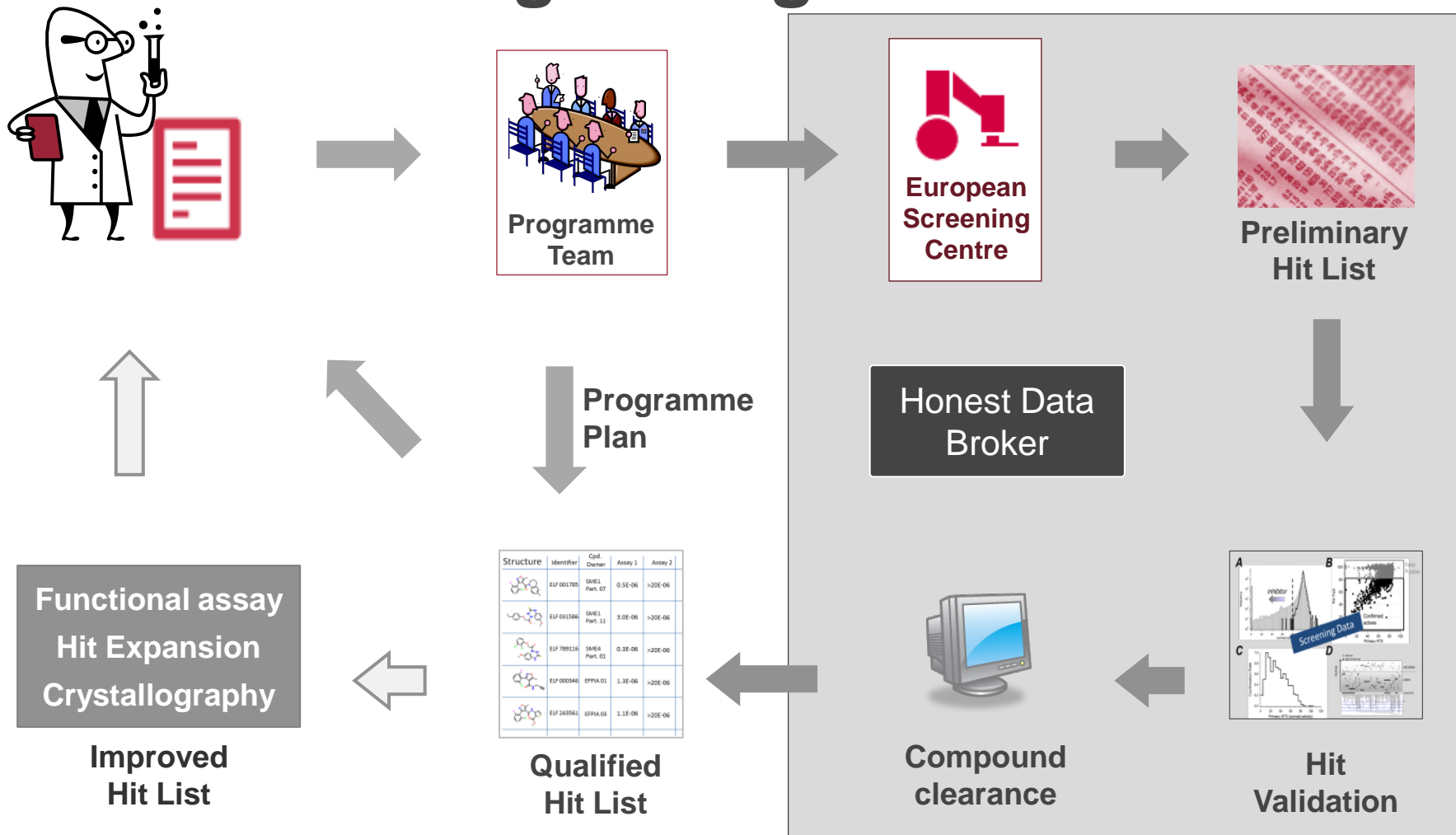
- **Value** determined by
 - Scientific **quality**
 - Innovation **potential** of target
 or
 - **new chemistry** associated with target
 - Disease **relevance**
 - **Diversity** of portfolio
- Technical **feasibility** of the assay
- **Transfer** to HTS in 3-4 months
- **Different** from EU Lead Factory targets



Review and Selection Process



Execution Target Programme



**Functional assay
Hit Expansion
Crystallography**

**Improved
Hit List**

**Qualified
Hit List**

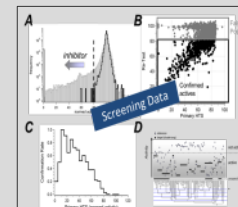
**Honest Data
Broker**

**European
Screening
Centre**

**Preliminary
Hit List**

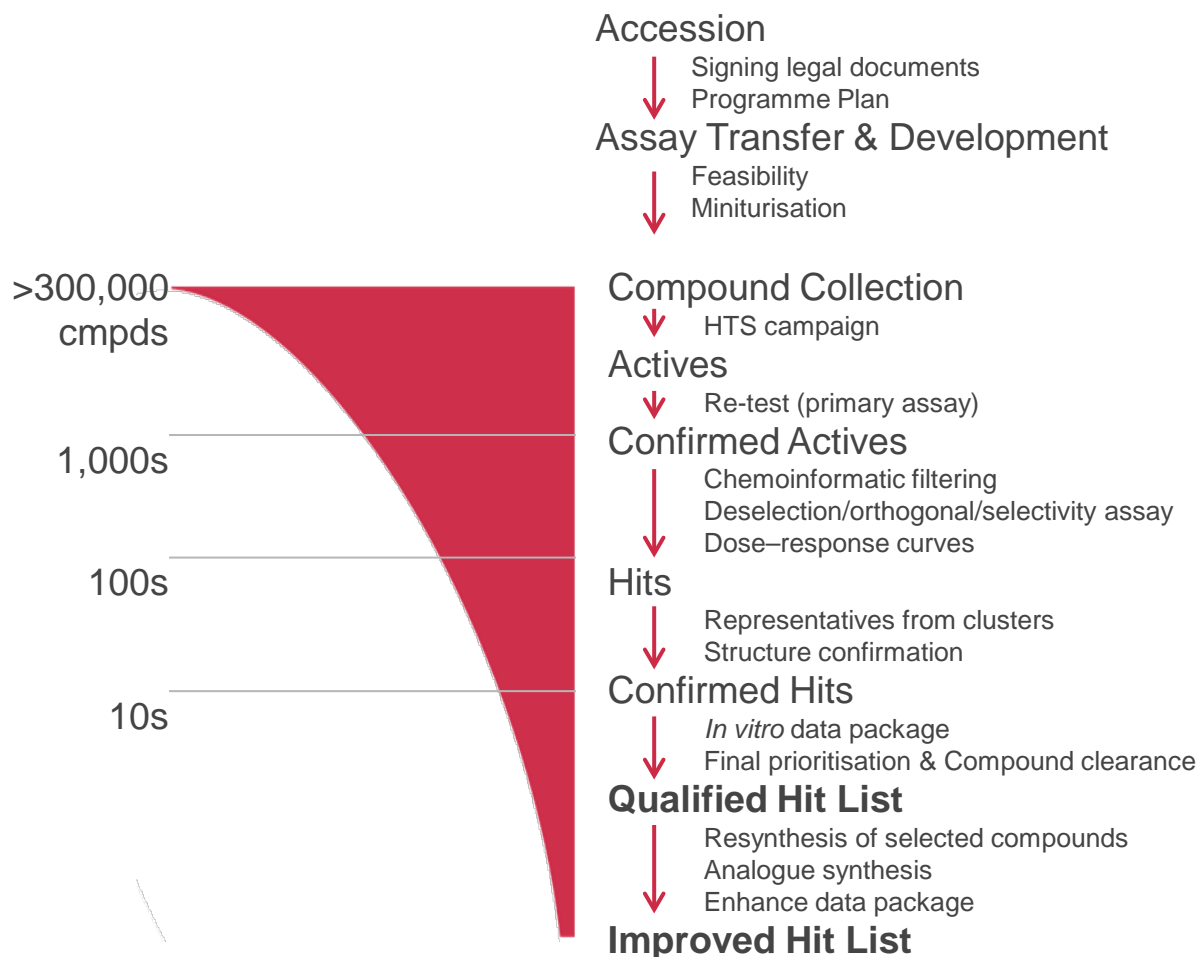


**Compound
clearance**








**Hit
Validation**

Public Target Programme **Process**

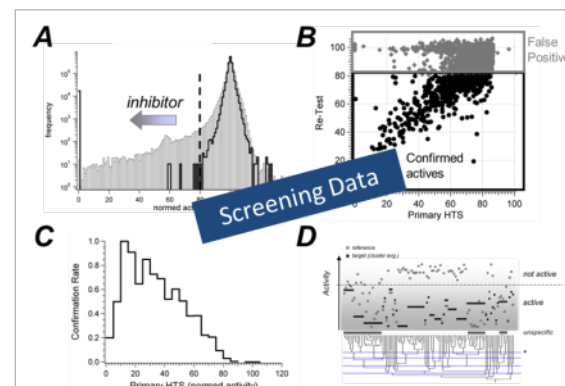


Deliverables Target Programme

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



Assay Miniaturization



Hit Statistics

Qualified Hit List
with associated
biological data



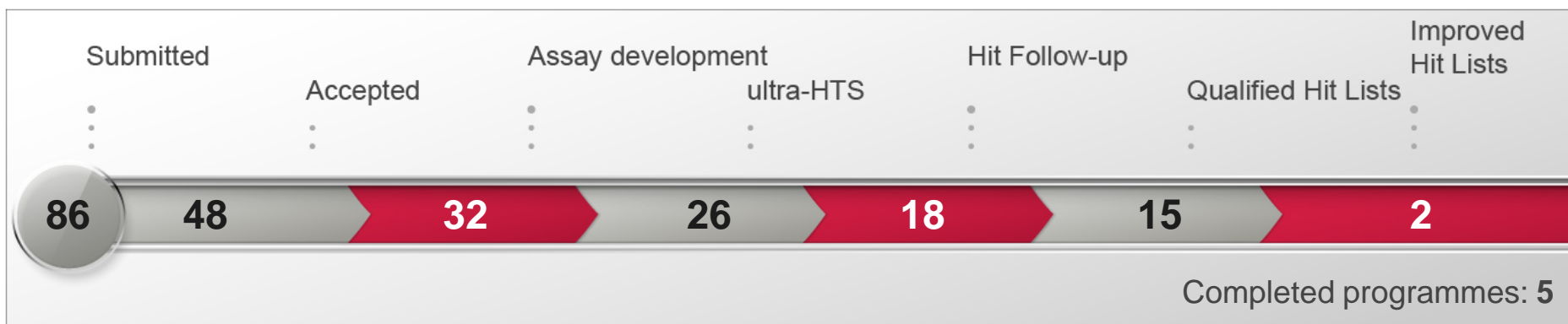
(Compound sample or
synthetic procedure)



**Preliminary
Hit List**

Public Target Programmes **Progress**

June 2015



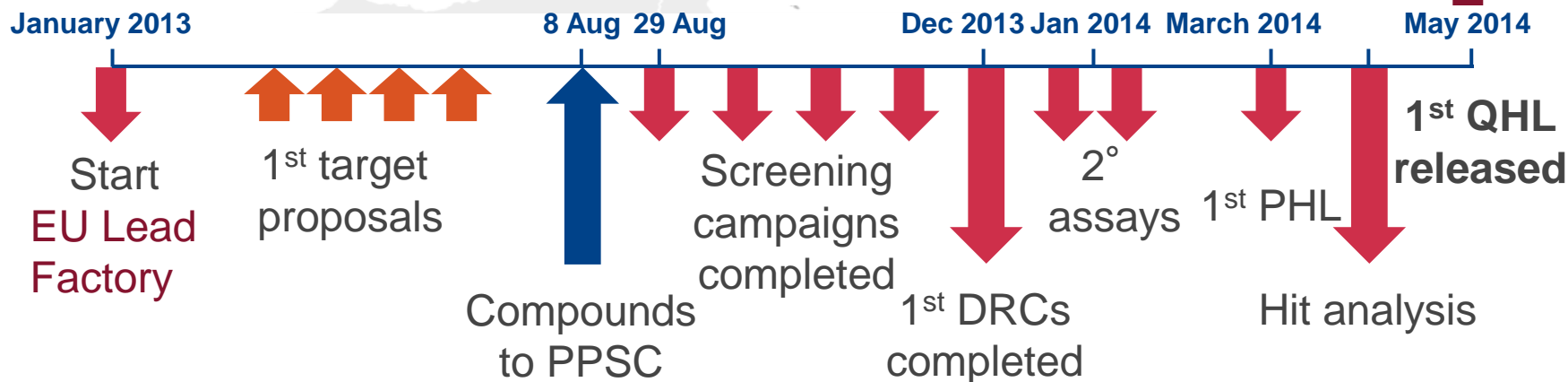
ESC in Action



*"Access to the European Lead Factory has **fast-forwarded** our drug discovery programme in the field of oncology **by several years.**"*



Dr Huib Ovaa, NKI



Example – Target programme



Case — University of Oxford



Process:

- Submission proposal 28 March 2013
- Accepted proposal 15 April 2013*
- Contract May 2013
- Assay transfer August 2013*
- *Ultra*-HTS (1536 wellplate format) October 2013
- Hit confirmation (1 **orthogonal** + 2 **deselection** assays) Nov 2013 - June 2014
- Transfer of Qualified Hit List Report October 2014



‘We could not realistically have got anything better.’

*‘The work done within ELF is really of **high industry-like standard** and **very professional**.’*

Post-QHL – Case

Early chemistry

- Prioritisation of chemistry by confirming active site competition using QHL samples
- 15 QHL compounds synthesised initially
 - All compounds flagged as definite binders (1) in SPR re-confirmed activity
 - None of the compounds flagged as non-binders (6) re-confirmed activity

Post-QHL – Case

Early chemistry

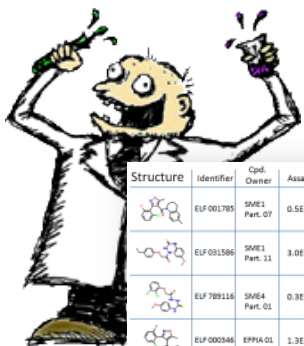
- Prioritisation of chemistry by confirming active site competition using QHL samples
- 15 QHL compounds synthesised initially
 - All compounds flagged as definite binders (1) in SPR re-confirmed activity
 - None of the compounds flagged as non-binders (6) re-confirmed activity

Current status - 5 months from release of QHL:

- Substantial SAR leading to rational design of pM compounds
- Crystal structure of 2 different series binding to target
- Excellent physchem and in vitro DMPK data on lead series
- On-target cellular efficacy



What happens after QHL delivery?



Structure	Identifier	Cpd. Owner	Assay 1	Assay 2
	ELF-001785	SME1 Part. 07	0.5E-06	>20E-06
	ELF-011586	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

**Qualified
Hit List**

**3-year exclusivity period
(Research or Direct Exploitation)**



First option to
EFPIA partners



**Milestone
Payments**

Publication Policy

Dissemination is encouraged!

Presentations

Scientific publications

Posters

Abstracts

Standard Reviewing Period

- **Clearance from the European Lead Factory team**
- **IP Protection**
- **No confidential data**
- **Conflicting interests**



Target assay owners'...

Rights

Screening of a unique
Compound Library at
Screening Facility

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

Full Control of Target
Programme Progression

Obligations

Access Rights and
Dissemination
(IMI's IP Policy)

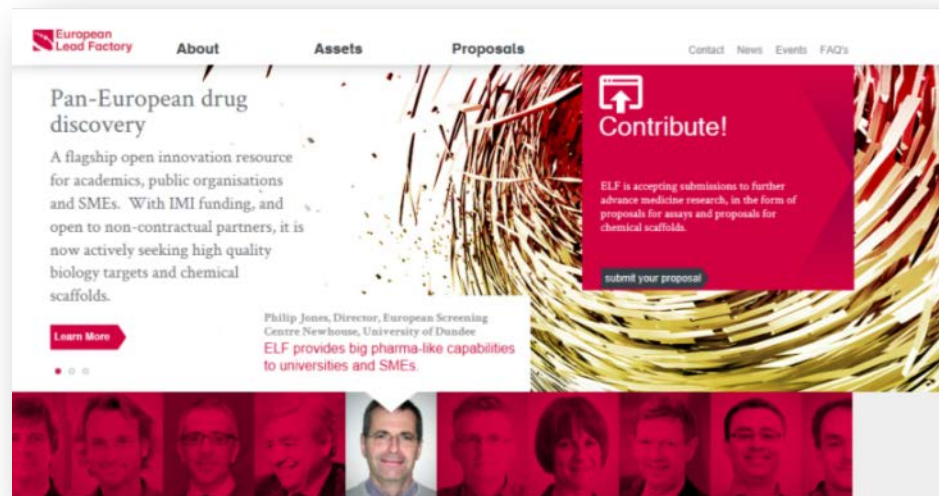
Compensation
to EU Lead Factory
- *for Direct Exploitation only* -

Option for EFPIA
to license Target Programme for
Direct Exploitation

Submit Your Proposal!

Website

www.EuropeanLeadFactory.eu



Linked in

EU Lead Factory LinkedIn Group

www.linkedin.com/groups/European-Lead-Factory

E-mail

Info@europeanleadfactory.eu



European Lead Factory

www.europeanleadfactory.eu

