



"Discovering The World Of Chemistry"



Dr. Dimitrios Tzalis

IMI Open Info Day: Horizon 2020 - Health, demographic
change and wellbeing

18th September 2015 Brussel





Taros: Stability, Capability, Flexibility

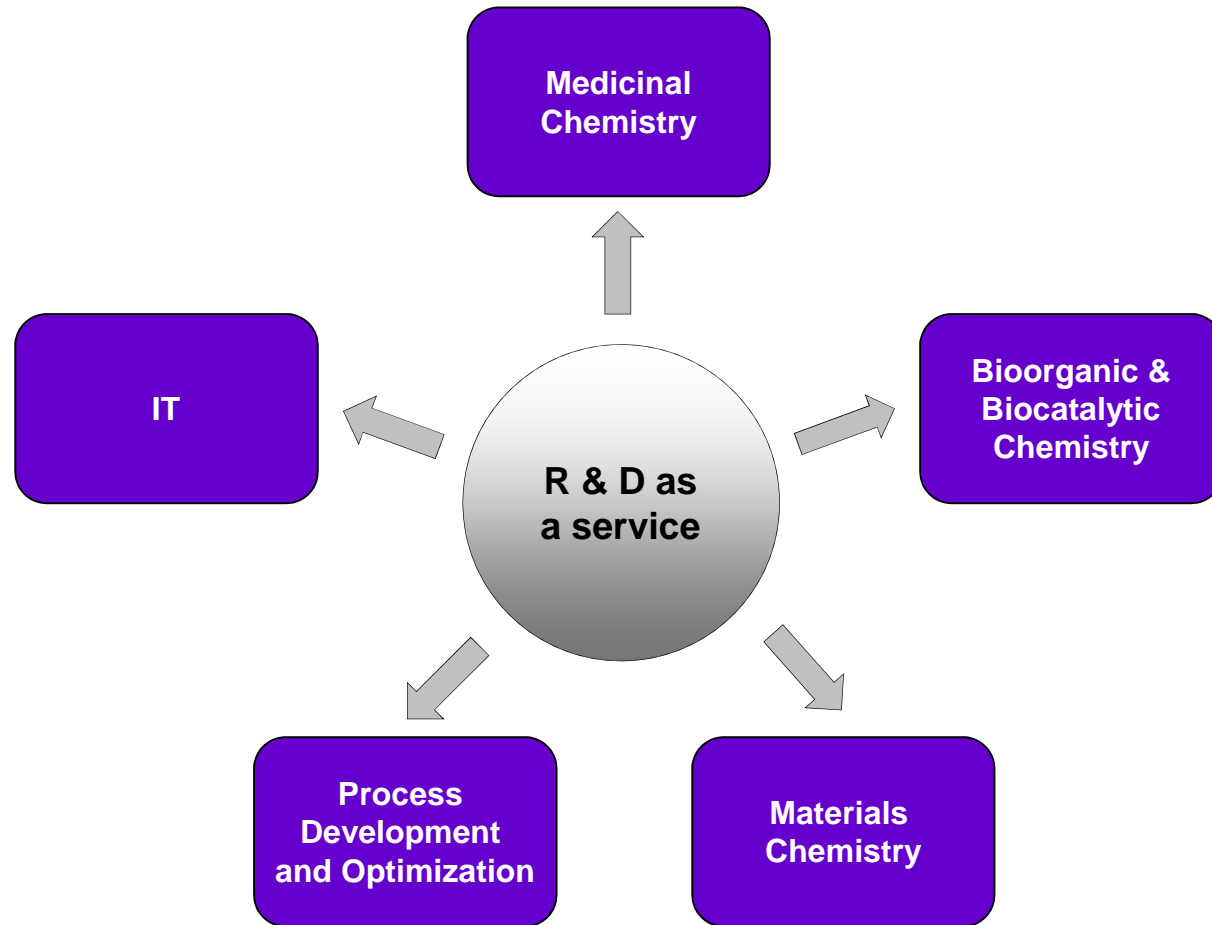
As a leader in drug discovery, Taros provides contract discovery, development, and manufacturing services to serve our clients' needs

- Founded 1999
 - Privately owned
 - 1500 sqm lab, based in Dortmund Germany (BioMedizinZentrum)
 - 62 employees (> 70% Ph.D.)
 - More than 6.000 projects delivered
 - More than 200 customers served
 - Invented "TarosGate", the smart 24h/7 Project Management Software
-
- **Taros is coordinating the Chemistry Consortium of the "European Lead Factory" drug discovery platform**





What do we actually do

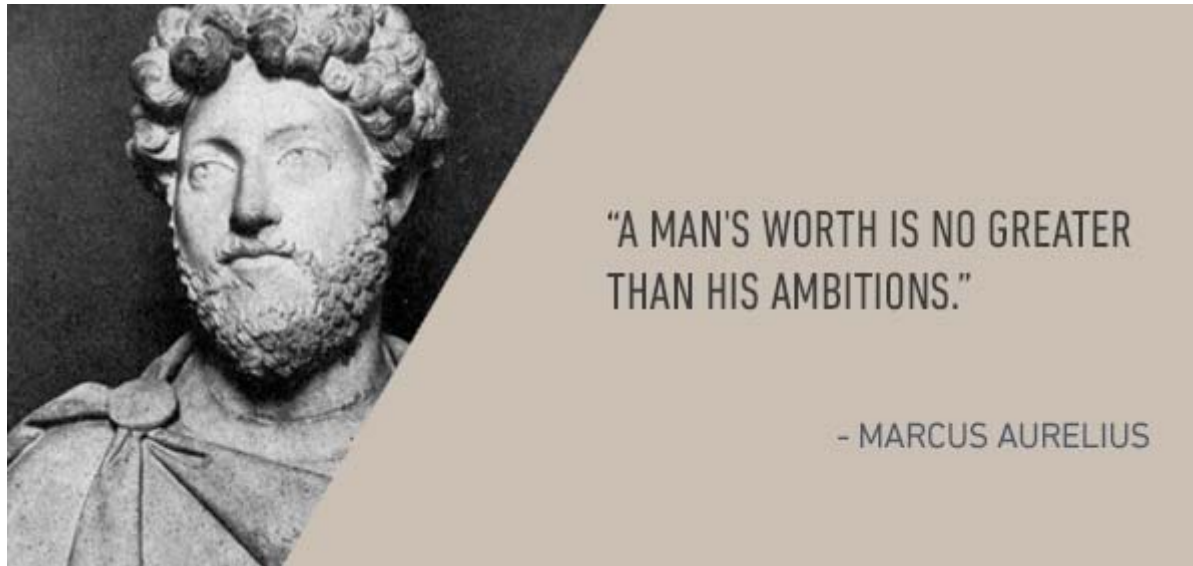


Pharma- and
CropScience Companies

Chemical Industry
(Materials)

Biotechnology
Companies

Research Institutes
and Universities



"A MAN'S WORTH IS NO GREATER
THAN HIS AMBITIONS."

- MARCUS AURELIUS

„A PROJECTS WORTH IS NO GREATER
THAN ITS AMBITIONS“



European Lead Factory

Game Changing for Innovative Medicine

Dr Dimitrios Tzalis, ELF Coordinator for the Public Compound Collection

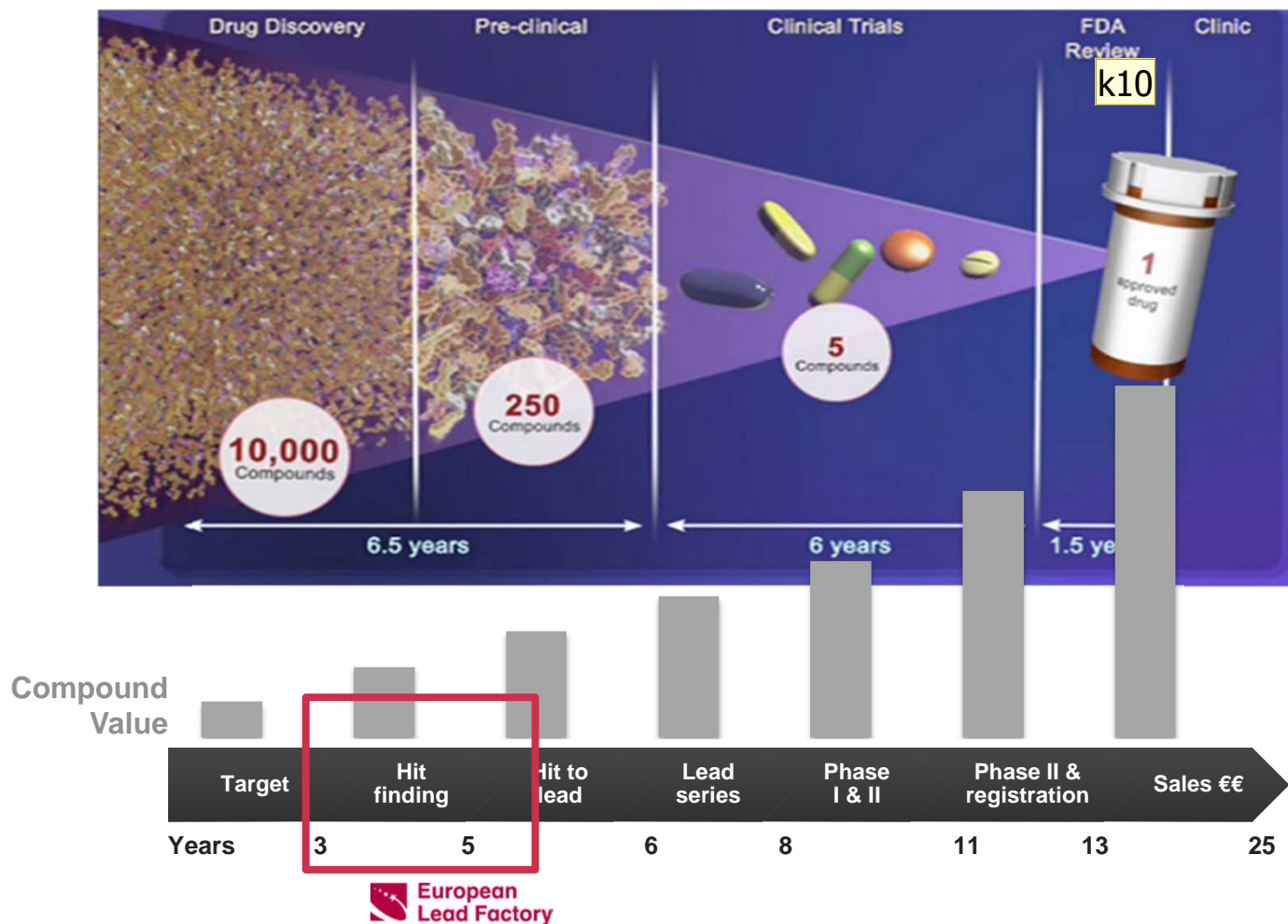
Open Info Day, 18th September 2015 Brussel

Consortium with 30 Public and Private Partners



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

Drug Research Value Chain

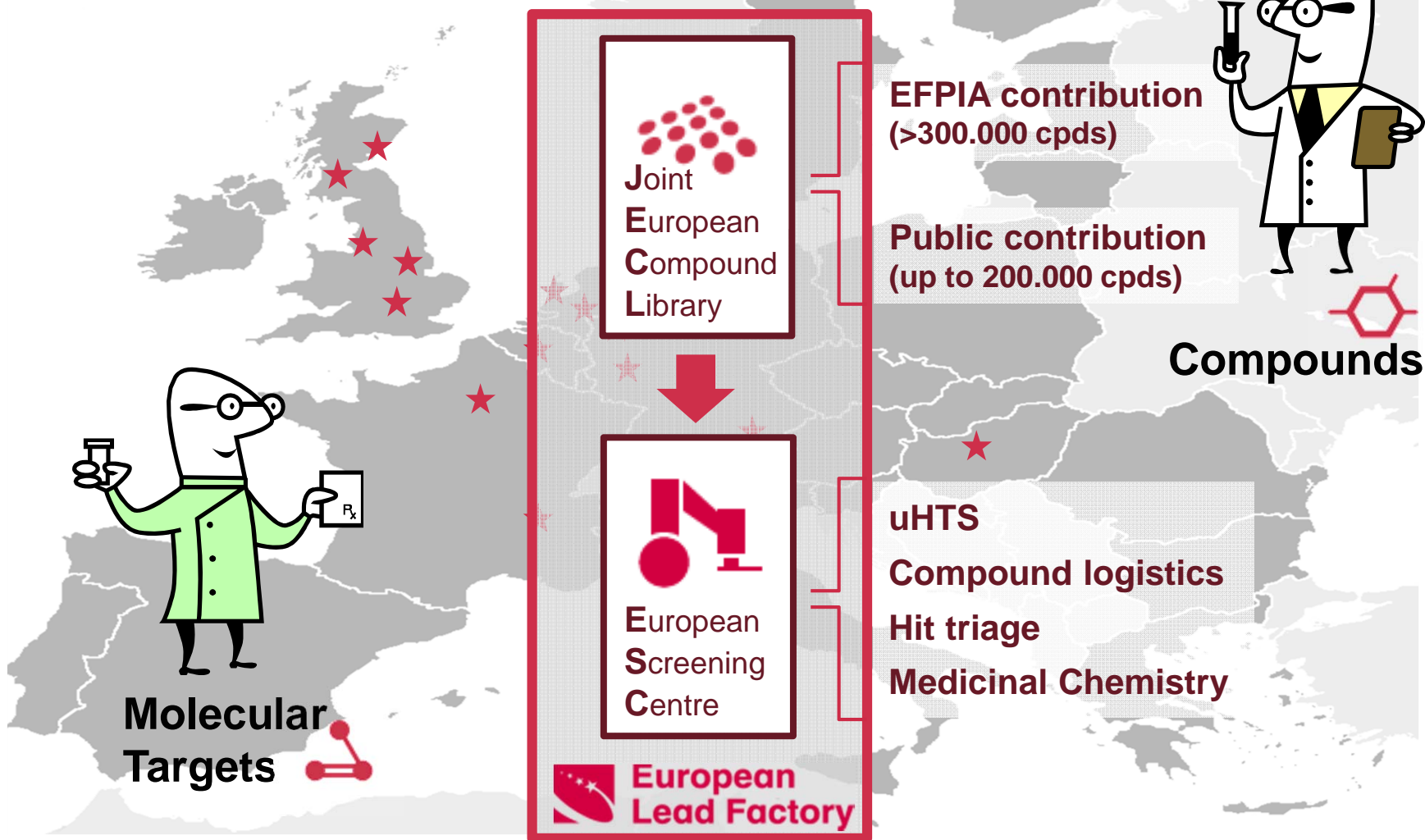


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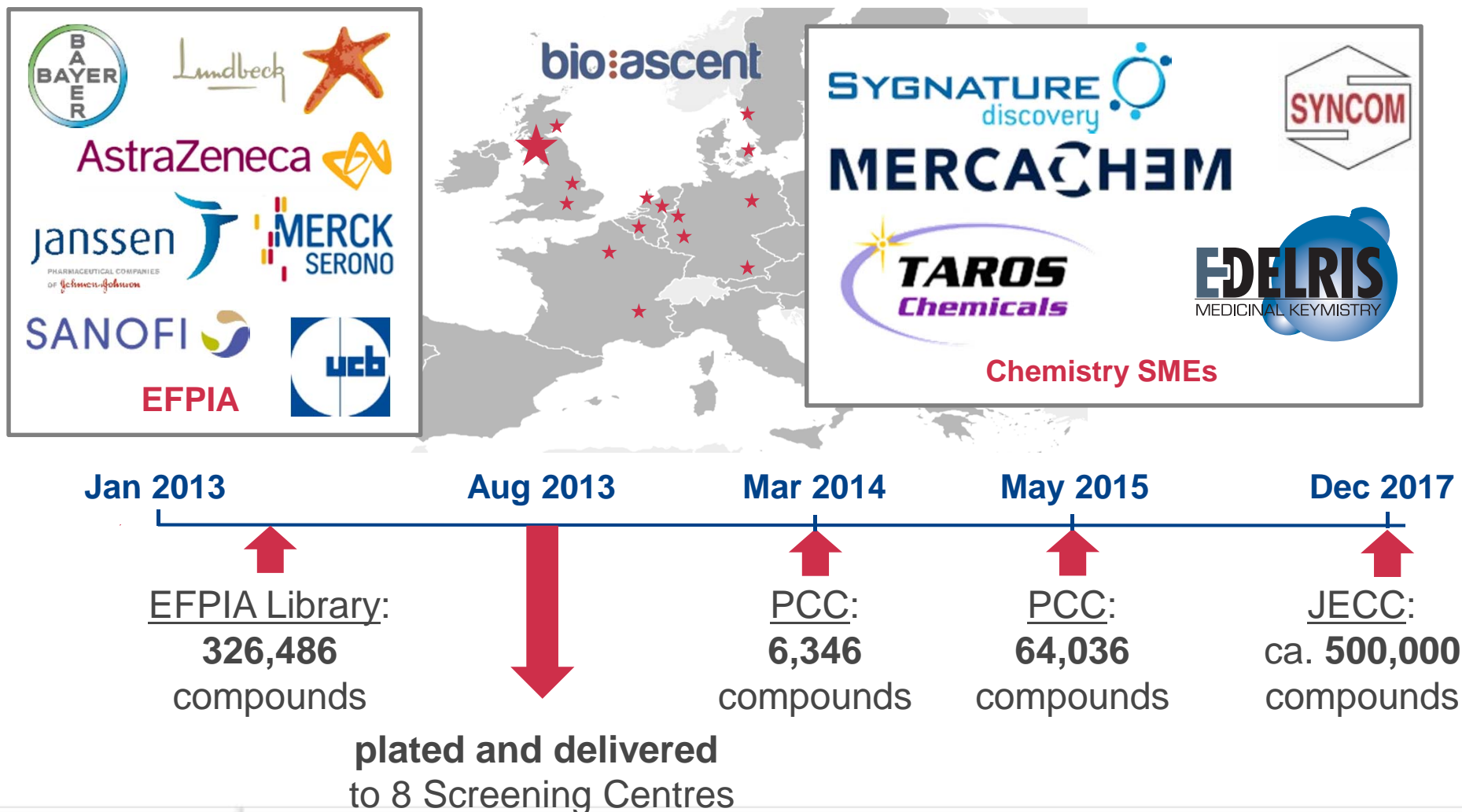
k10

FDA should read EMA
kristina.orriling, 28/05/2014

Collaborative Drug Discovery Plattform

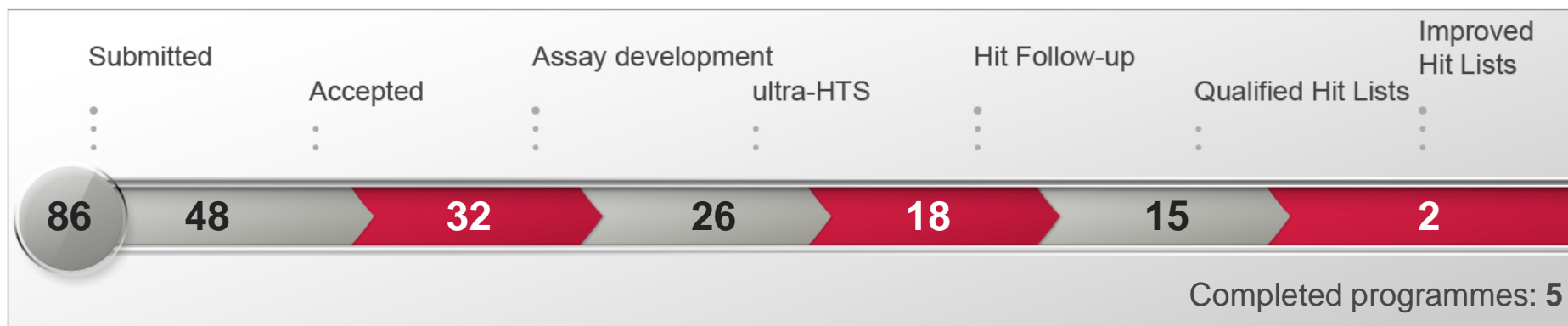


Building the JECL



Screening Achievements since 2013

- All relevant technical capabilities operational
- Core EFPIA library available for screening
- Honest Data Broker system available for protected data handling
- Lines of communications to coordinate screening partners established
- Efficient recruitment and selection process of high quality programmes in place
- Education of academic programme owners during entire process
- High quality output of screening and hit validation



Results

Design, synthesis and decoration of molecular scaffolds for exploitation in the production of alkaloid-like libraries

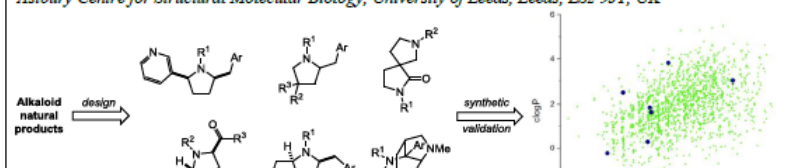
Philip Craven¹, Anthony Aimon², Mark Dow³, Remy Morgentiu⁴, Didier Roche⁵, Tuomo Kalliokoski⁶, Richard Foster⁷, Stephen P. Marsden⁸ and Adam Nelson^{3,4}

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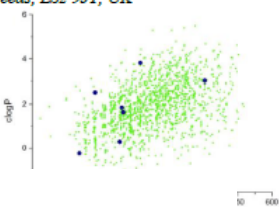
A Universal Isocyanide for diverse Heterocycle Syntheses

Patil Parvin,¹ Kareem Khoury,² Eberhardt Herdtweck,³ Alexander Dömling^{1*}

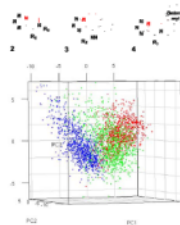
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ABSTRACT



Novel scaffolds are of utmost importance for the discovery of functional material. We describe three different heterocyclic scaffolds easily accessible from isocyanacetamide-derived dimethylacetamide 1 by multicomponent reaction

NATURAL PRODUCT-INSPIRED LIBRARIES FOR EXPLOITATION IN THE EUROPEAN LEAD FACTORY

Mark Dow, Steve Marsden, Richard Foster and Adam Nelson

School of Chemistry, University of Leeds, LS2 9JT, UK. Presenting author email address: M.J.Dow@leeds.ac.uk. Nelson group webpage: www.sci.leeds.ac.uk

What is the European Lead Factory (ELF)?

- ELF is designed to create opportunities for the discovery of new lead molecules through a collaborative consortium of pharmaceutical companies, academic organisations, small-medium enterprises (SMEs) and public bodies.
- As part of the project, the unique Joint European Compound Library (JECL) is being
- To complement the 300,000 compounds provided by the consortium's pharmaceutical company partners, an additional 200,000 distinctive new compounds will be produced using innovative synthetic approaches.
- Proposals for libraries of distinctive new compounds ("Library Design Proposals") formed from academic groups and SMEs, and may be contacted at: elf@leeds.ac.uk. The synthetic validation work described production of two large libraries by our SME partner.

From Cyclic Imines to Nitrogen-Rich Scaffolds through Multicomponent Sequences

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What is the European Lead Factory (ELF)?

The ELF is a pan-European platform for drug discovery, supported by IMI, which was set up to give a major boost to drug research in Europe. It is the first pharmaceutical and life science partnership of its kind and has been designed to create unparalleled opportunities for the discovery of new drug lead molecules.

The pharmaceutical companies in the consortium have contributed a total of over 300,000 compounds to the project in order to create a joint compound collection. An addition of estimated 200,000 novel compounds is currently being generated by public partner contribution during the project, resulting in a unique Joint European Compound Library with some 500,000 compounds.

The ELF combines the power of the pharmaceutical industry's previously inaccessible compound libraries with the innovation offered by the academic community when designing novel compounds and with the expertise of many SMEs in MTL and library generation. Importantly, it will provide a screening platform of industrial excellence in Europe for small molecule drug discovery projects in the public sector.

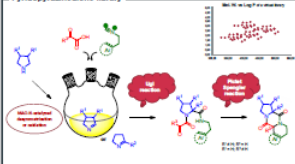
Our contribution

Our contribution to the consortium consists of the design of new libraries of compounds based on our expertise in isocyanide-based multicomponent reactions (MCRs), which provide several points of variation in one single operation.

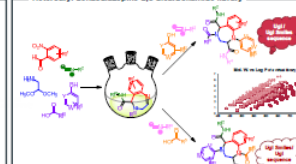
We have previously reported several examples that efficiently combine the MAD-NO-catalysed deprotection of cyclic imino-amines with MCRs and lead to interesting profile derivatives.

Herein, we present new sequences of MCRs, employing various cyclic imino as key intermediates for the efficient construction of diverse nitrogen-rich scaffolds such as pyrrolidines, piperazines, hexahydroindolizines and quinoxaline derivatives.

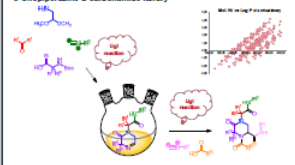
Pyridopyrazinone library



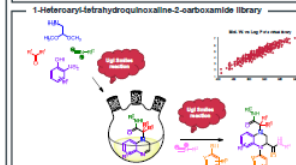
Heteroaryl-benzodiazepine-2,6-dicarboxamide library



6-Oxopiperazine-2-carboxamide library



1-Heteroaryl-tetrahydroquinoxaline-2-carboxamide library



References

1. M. Dow, A. Nelson, P. J. J. Holmes, V. Helwell, M. Turner, N. J. Orr, R. V. A. Orru, *Chem. Sci.* 2016, 7, 2084-2090.
2. M. Turner, N. J. Orr, R. V. A. Orru, *Chem. Commun.* 2016, 46, 7588-7590.
3. M. Turner, N. J. Orr, R. V. A. Orru, *Org. Biomol. Chem.* 2012, 10, 101-104.

Acknowledgements

The research leading to these results has received support from IMI under grant agreement n° 115489 and EFPIA companies in kind contribution.



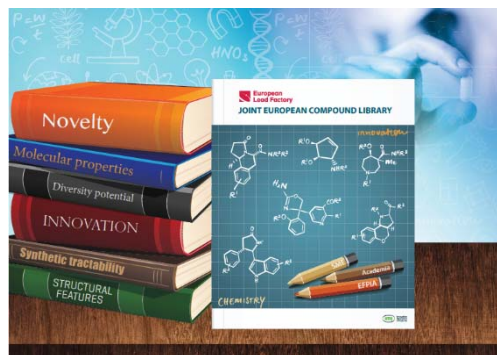
Innovation

Symposium-in-print in *Bioorganic & Medicinal Chemistry Letters* features **13 papers** from consortium partners [(2015) **23**(11), 2607-2740]

- Highlights innovative synthetic approaches (eg. natural product-like libraries, multi-component approaches and diversity-oriented synthesis)

Invited article in *Drug Discovery Today* [(2015) *accepted*] and two invited book articles

- Highlights innovative molecular properties and uniqueness of produced compounds (eg. structural, physicochemical, conformational)





EUROPEAN LEAD FACTORY

www.europeanleadfactory.eu

SME: how to participate in an IMI call



Join Our Network

2 Options

- create and coordinate a consortium
- join a consortium

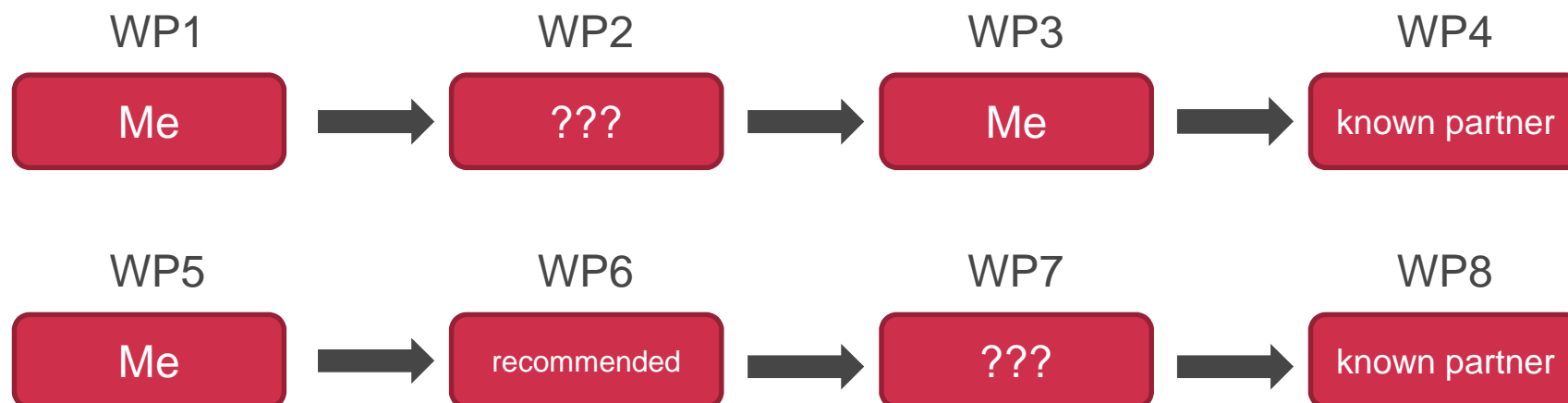
Application Phase



Application Phase

First problems to encounter:

- Search: who fits into a potential consortium



Application Phase



What is important when considering a new partner

- search should be INTERNATIONAL
- partner should be contributing proactive
- but first and foremost: the chemistry has to be right

SME: Grant Application

- follow exactly the call text
- close gaps that you have through partners
- if not sure clarify ahead of proposal submission

Do you need pre-existing experience in FP 7 to participate or coordinate an IMI Call?

- NO

but: IT REALLY HELPS

- there should be pre-existing experience with local and national funding agencies
- proper accounting and documentation procedures have to be in place

Do you need pre-existing experience with Big Pharma to participate or coordinate an IMI Call?

- NO

but: IT REALLY HELPS

- The goal of IMI calls is to generate VALUE by translating academic knowledge into (commercial) value (close in time and not some time in the future)
- Coordinator is a EFPIA representative

What about IP protection?



- IMI has laid out in the Grant Agreement clear rules and all builds on these
 - Focus is that everybody has his/her IP/value protected
 - Fair treatment of all partners
 - Exploitation of generated IP is a question of negotiation

Legal Issue: Project Agreement



- EFPIA and academia arrived with an „Armada“ of highly experienced and competent lawyers
- essential in the application phase was a legal advisor (could be difficult for SMEs)
- we where 5 SME who shared costs for a legal advisor

Do you need external advisors supporting you in the IMI call?

YES!!!

- highly recommended: especially for SMEs
- highly experienced and provide infrastructure supporting the application - and project phase (reports, finance, formalities)
- normally free of charge during the application phase

How does IMI compare to „traditional“ programmes

- EFPIA is strongly involved
 - goal: generate value (value does not always mean €€)
 - intensive exchange with EFPIA in order to assure real application
- optimal utilization of:
 - creativity of academia
 - flexibility and agility of SMEs
 - efficiency and vision of the „Big Pharma“
- it does not focus solemnly on the need of one partner but it is focused on one aspect:

The greater good of the patients and society

Things to look out for and be cautious



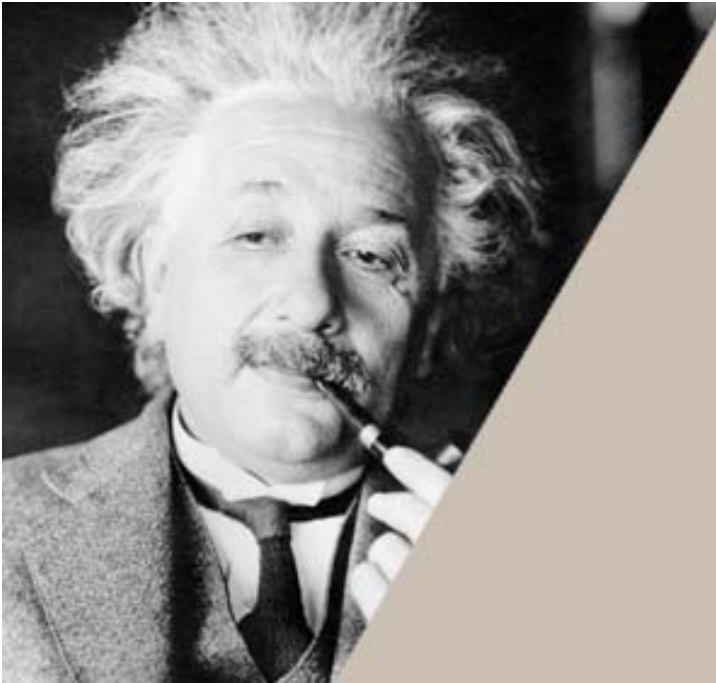
- overwhelming personalities
- company has to be financially sound
- ramp up phase should be kept short

Benefits for SME in the participation in the IMI

- intensive exchange with EFPIA
- insight in requirements and operation of EFPIA partners and the needs of academic partners in the field of drug discovery
- partnerships and trust is being built
- loose cooperation on „equal“ grounds
- access to a wide network of other SMEs, academic partners and big pharma representing potentially an entire Drug Discovery Value Chain

Lessons Learned





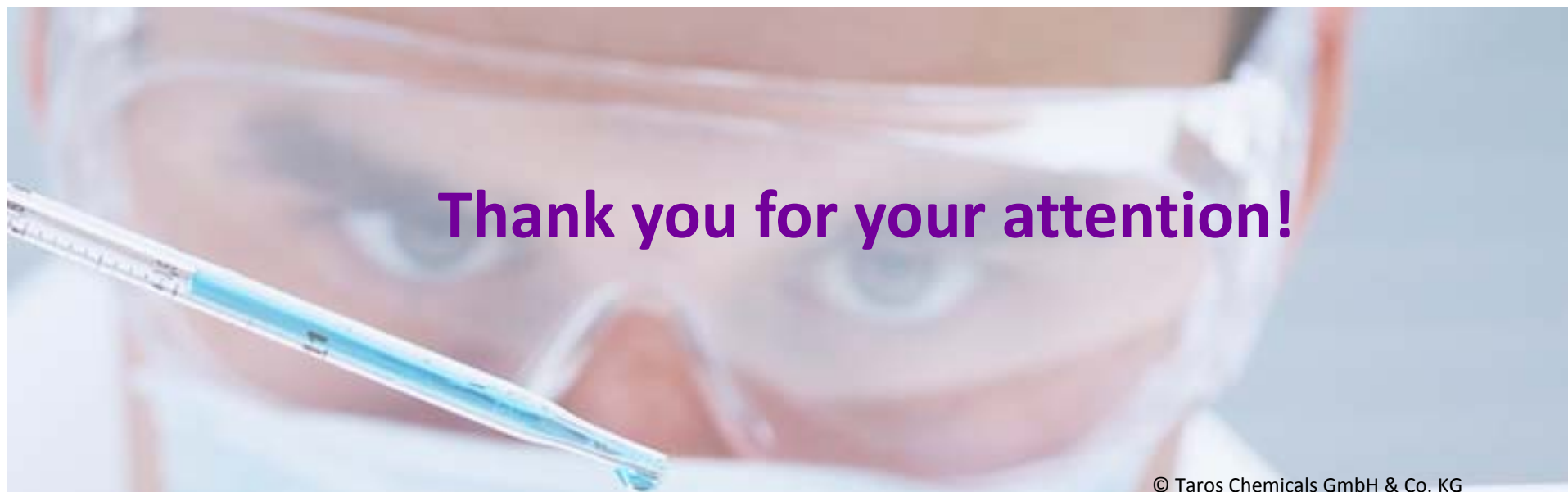
“TRY NOT TO BECOME A MAN OF
SUCCESS, BUT RATHER TRY TO
BECOME A MAN OF VALUE.”

- ALBERT EINSTEIN



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ANY QUESTIONS?

