



**COLLABORATIVE  
DRUG  
DISCOVERY**



# **RESULTS, IMPACT AND OUTLOOK OF THE IMI EUROPEAN LEAD FACTORY**

January 2019



**European  
Lead Factory**



**efpia**

“The European Lead  
Factory is leading  
the way to discovering  
new medicines”

[http://ec.europa.eu/research/infocentre/article\\_en.cfm?artid=47596](http://ec.europa.eu/research/infocentre/article_en.cfm?artid=47596)

This is the executive summary of the final report prepared by the EUC2LID consortium and approved by its funding organization, the Innovative Medicines Initiative Joint Undertaking. The research leading to the results presented in this report has received support from the IMI-JU 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.

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COLLECTIVE  
INTELLIGENCE





## EXECUTIVE SUMMARY

### *Seeding tomorrow's priority medicines*

The European Lead Factory was set up to accelerate the long, complex and expensive process of drug discovery that is critical to developing innovative medicines for global health challenges. In 2013, seven large pharmaceutical companies decided to pool compound collections and open them up to academia and small- and medium-sized enterprises (SMEs) searching for drug discovery starting points. With the support of Innovative Medicines Initiative (IMI), a public-private partnership was established with a 5-year budget of EUR 196 million to create a shared asset for open innovation. Since then, the European Lead Factory has successfully composed a library of over 500,000 compounds (of which 200,000 were designed and synthesized de novo), crowdsourced 88 disease targets from the scientific community and delivered close to 200 qualified or even improved hit lists as starting points for new drug discovery programmes - as well as 5 patents, 2 partnering deals, and close to 90 peer-reviewed scientific publications. The results to date confirm that the European Lead Factory can indeed advance biological concepts into drug discovery projects that benefit academia, industry and ultimately society.

### FAST FACTS ABOUT IMI'S EUROPEAN LEAD FACTORY

- Aim: To provide quality lead compounds for innovative disease-related targets
- IMI funding term: January 2013 – May 2018
- Total budget: 196 M€, i.e. 80 M€ (IMI) + 91 M€ (pharma partners in-kind) + 25 M€ (public partners in-kind)
- 30 participants = 13 academic + 10 SMEs<sup>1</sup> + 7 pharmaceutical companies<sup>2</sup>
- 150 public partner employees involved
- Any researcher at any European SME or academic institute could take part as target owners or chemical library designers
- Researchers in 15 countries (AT, BE, DE, DK, ES, FI, FR, IT, IL, HU, NL, PL, PT, SE, UK) directly involved. Partners spread over 8 countries and target owners over 13.

<sup>1</sup> SME = small or medium-sized enterprise

<sup>2</sup> Members of EFPIA (European Federation of Pharmaceutical Industries and Associations)

<sup>3</sup> Creating a novel Public Compound Collection, as part of the Joint Compound Collection, based on differentiated design principles and/or targeted to difficult target classes.

## 1.1 PROJECT RATIONALE AND OVERALL OBJECTIVES OF THE PROJECT

*The European Lead Factory set out to create a shared platform for collaborative drug discovery*

Despite significant scientific advancements, many medical needs remain unmet. Drug discovery is a long, complex and expensive process that starts with identifying chemical compounds or biological molecules that can modulate a drug target involved in the disease course. Attrition is high over the whole development chain, with only a fraction of drug discovery programmes advancing to clinical development, let alone reaching the market. The European Lead Factory was set up to increase the speed and success of the critical first step (see Figure 1). It combines industry's expertise and experience with the innovative strength of the European academic life science community and the agility and creativity of small- and medium-sized enterprises.

### SUMMARY OF OBJECTIVES

The overall objectives of the European Lead Factory (ELF) were to:

- **Create an industry-standard screening collection** by pooling selected compounds from the proprietary collections of industry ("big pharma") participants and complementing this Joint European Compound Library (JECL) with novel compounds from ELF's own synthesis programme<sup>3</sup>;
- **Open it to third parties** from European academia and biotech small- to medium sized enterprises to screen their targets through a crowdsourcing action;
- **Provide access to ultrahigh-throughput screening (uHTS)** facilities in a European Screening Centre (ESC), allowing co-creation of new drug discovery programmes;
- **Identify "Qualified Hits"** within defined discovery programmes for further optimization into lead structures or research tools (using the JECL, ESC and industry screening facilities);
- **Generate and share knowledge** to provide guidance to the drug discovery community on successful strategies in library design and in lead discovery techniques; and thus
- **Establish a shared platform for collaborative drug discovery** that fosters partnerships between public and private sectors as well as between EFPIA<sup>4</sup> partners and service providers in early drug discovery.



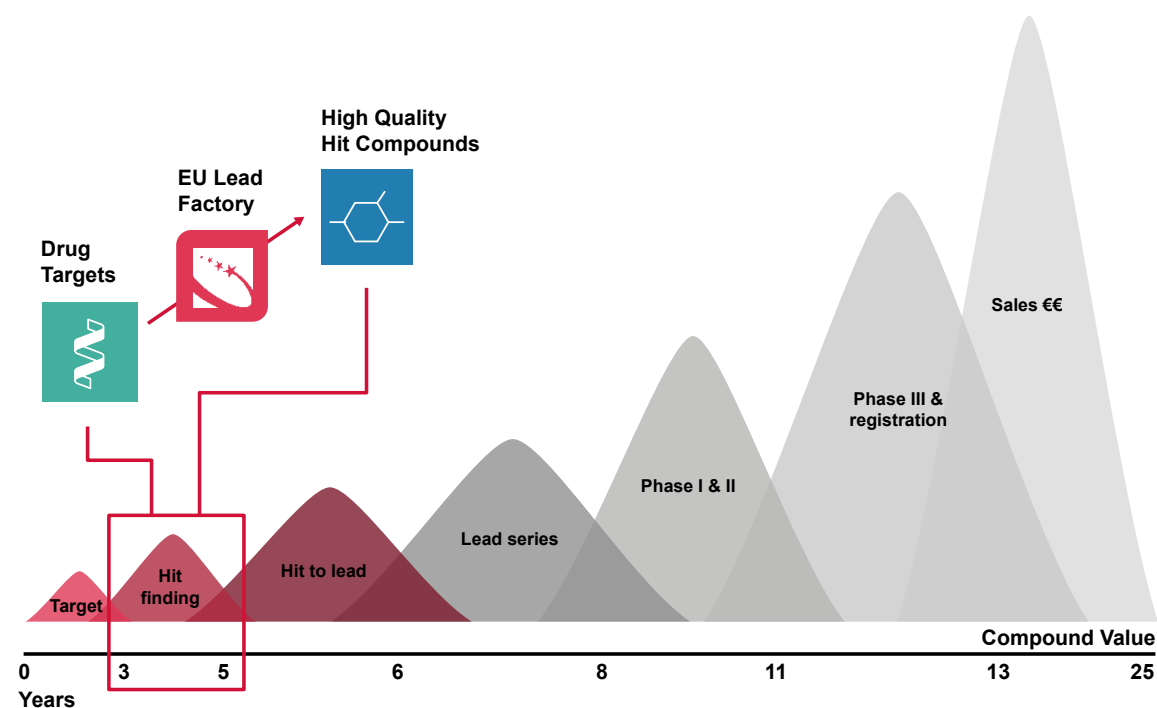


Figure 1. The position of the European Lead Factory in the drug research value chain.

## 1.2 OVERALL DELIVERABLES OF THE PROJECT

*The European Lead Factory catalyses the discovery of new medicines for some of the biggest health challenges*

The ELF combines complementary industry and crowdsourced portfolios to address unmet medical needs and create critical mass to eventually delivering a medicine to the patient (see Figure 2).

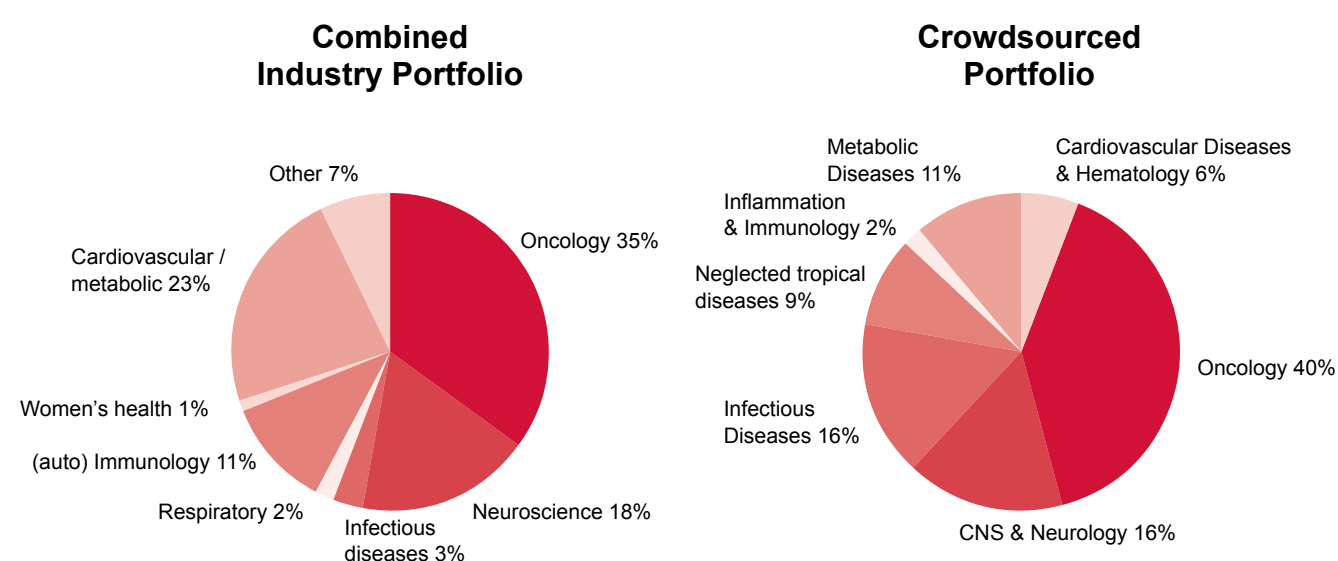


Figure 2. The European Lead Factory addresses therapeutic areas with high unmet medical needs. The distribution of the ELF industry (left) and crowdsourced (right) portfolios are complementary.

The European Lead Factory has already delivered results in all therapeutic areas, including some of the world's biggest health challenges:

**Cancer.** The second cause of death globally, cancer rates are still rising. The growth and ageing of our world's population alone leads to an expected 21.7 million new cases and 13 million deaths per year in 2030.<sup>4</sup> Unhealthy lifestyles (smoking, poor diet, lack of exercise) and changing demographics in the developing world will likely make the future cancer burden on society much larger still.

**Metabolic disorders.** These are well-known risk factors for both cardiovascular diseases and cancer, and on the rise across the globe. Diabetes alone is predicted to inflict disease in 592 million people by 2035.<sup>5</sup>

**Neurodegenerative diseases.** Diseases such as Alzheimer's and Parkinson's are directly delated to ageing and present societies with a huge economic and human resource challenge.

**Antimicrobial resistance.** Possibly the biggest threat on the horizon. As a globalized world makes it ever more difficult to contain highly-infectious diseases and (over)use of antibiotics breeds resistant "superbugs", future outbreaks could be hugely disruptive - even to first-world countries.

**Neglected tropical diseases.** It is a particular challenge to discover and develop new medicines for neglected tropical diseases and to provide access to medicines in (developing) countries having poor infrastructure and small means - even as globalization and climate change spread the threat of these diseases to the developed world, as well. Examples are African sleeping sickness, leishmaniasis, Chagas disease and dengue fever.

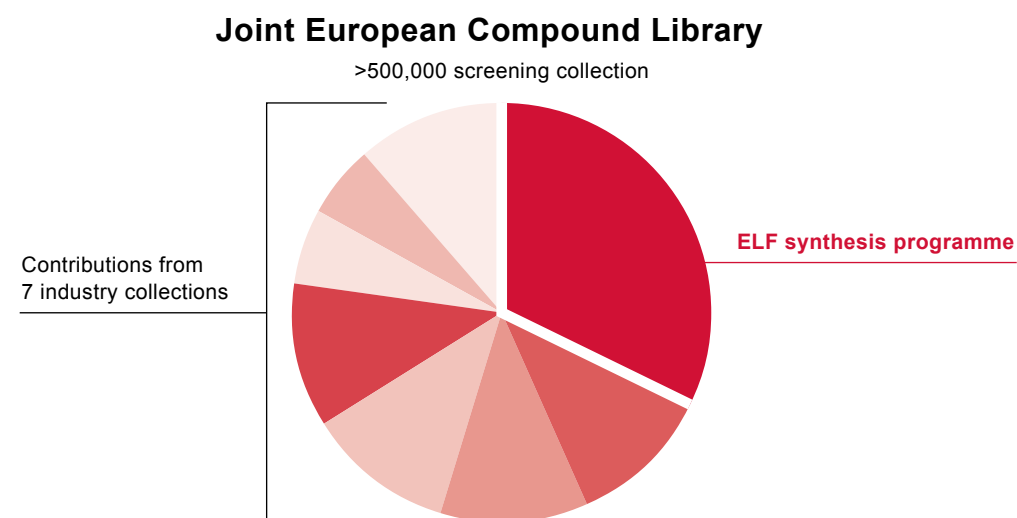
We have included case examples of ELF successes for these diseases in section 1.4. These successes are possible because the European Lead Factory has delivered an operational platform, tangible results for its users, follow-up work, and education and networking.

<sup>4</sup> American Cancer Society. Global Cancer Facts & Figures 3rd Edition. Atlanta: American Cancer Society; 2015.

<sup>5</sup> International Diabetes Federation. IDF Diabetes Atlas, 6th edn. Brussels, Belgium: International Diabetes Federation, 2013.

*An operational platform: Joint European Compound Library and European Screening Centre*

The European Lead Factory created the Joint European Compound Library from over 320,000 compounds contributed by seven pharmaceutical industry partners and added 200,000 novel compounds from its own synthesis programme (see Figure 3).



**Figure 3.** The composition of the Joint European Compound Library (JECL).

Ideas for compounds to be synthesised were submitted through a specially designed web-tool (see section 1.5) and assessed against specific criteria, including novelty, diversity potential, drug-likeness, and synthetic tractability. Out of more than 1,000 submitted designs, 666 proposals were accepted, validated (for scalability and robustness) and further refined before production to maximize their diversity, optimise properties and ensure novelty against public and commercial compound sources and ELF's own growing library. Over 200,000 library compounds meeting the quality criteria for purity (LM-MS purity>85%) and quantity (5>mmol) were subsequently added to JECL. In an analysis comparing the physicochemical properties of the ELF compound library with commercial collection (Maybridge), it was found that the ELF library was more alike biologically active compounds (ChEMBL), reflecting the compounds' drug-likeness.<sup>6</sup> These novel compounds have proven their value by showing up in qualified hit lists and being selected for follow-up work – and increasingly so, as more are added to the screening deck and exposed to targets.

To use the JECL to screen targets and find hits, ELF has established a pan-European infrastructure for ultrahigh-throughput screening (uHTS) – an approach proven to be superior for finding small molecules to start drug discovery programmes.<sup>7</sup> Industry partners use their own screening centres. The crowdsourced programmes are executed by the independent European Screening Centre. In total, over 200 target programmes have been selected and scheduled for screening in ELF. A tailored approach was taken to each crowdsourced programme, with unique workflows and different assay types. The European Lead Factory supports nearly all HTS-compatible assay techniques, but an ELF programme consists of much more than an initial screen. In some cases, or more follow-up screens were completed to ensure the selection of compounds returned to the programme owner was of the highest possible quality.

**“The European Lead Factory represents a fantastic opportunity to see the molecules prepared in our synthetic projects make a genuine impact in medicinal chemistry. To know that our products may one day help address some of society’s greatest health challenges like cancer or antimicrobial resistance is extremely satisfying and exciting!”**

**Dr William Unsworth**  
University of York

In June 2018, it was estimated that there were more than 150,000,000 data points associated with screening in ELF. The diversity of these data is unprecedented in any drug discovery setting. Just for the crowdsourced targets, more than 280 bespoke biochemical, cellular and biophysical assays were developed for, and in several cases together with, the programme owner.

#### *Tangible results*

In using and sharing these assets, the European Lead Factory has demonstrated the potential of a novel, network-type model of early drug discovery at the interface with traditional competitive medicine research. The first qualified hit list (QHL) was delivered in May 2014 and since then 160 - almost half led by public institutes or young biotech companies - have followed and received a boost of over 8,500 small molecules in total. In addition, another 47 programmes have been initiated with deliveries of results pending at the time of writing. Encouraging results have produced lead compounds, even candidate drugs, scientific publications in journals, PhD theses, patents, new collaborations, academic spin-out companies, and a charity-funded virtual biotech. We expand on these results in more detail in section 1.5.

#### *Value creation for programme owners*

The full impact of the ELF outcomes is yet to be seen. As a first indication, we can focus on the 23 programmes crowdsourced in the first year. They represent a quarter of the crowdsourced portfolio. All targets proved feasible to screen and QHLs were delivered to the programme owners. For 18 of these 23 programmes (>75%), the scientific data was promising enough to warrant further follow-up work. Three programme owners decided to progress the results independently. Nine of the programmes followed-up within the framework of ELF have resulted in highly active analogue compounds validated with biochemical, biophysical, and in vivo data. So far, ELF results have led directly to further funding for six programmes, four patents, two start-ups and two major partnering deals with pharmaceutical companies outside the consortium. For the industry partners, 119 drug targets led to 105 screening campaigns and 89 QHLs. For 29 (30%) of these programmes, follow-up laboratory chemistry work has been initiated to validate results by resynthesizing hits and generating analogues. Three have already progressed to the lead optimisation stage, typically the most resource-intensive phase in drug discovery. These results vindicate the industry partners' decision to open up their libraries and are so promising that they have decided to support a project building on ELF's legacy.

#### *Education and networking*

In addition to these tangible outcomes, many academic and biotech target owners gained valuable experience with the drug discovery process and industry-like execution of screens. ELF also organised several types of knowledge-exchange events. Four meetings were dedicated to support and encourage proposals for both targets to be screened against JECL and ideas for novel compounds to be synthesized. The academic and industry chemistry partners met up at five so-called Learning & Achievements Events, whereof the last three of which were open to early career researchers. These not only led to some high-quality submissions but established and enhanced networks. In the last three years, programme owners and other stakeholders were welcomed to join the annual consortium meeting. For many target owners, the European Lead Factory provided a low-threshold entry point for engaging in a pan-European public-private partnerships and for forming new alliances.



**“My time as part of the European Lead Factory was not only stimulating, challenging and enjoyable, but it was also instrumental in securing me a job as a medicinal chemist in industry.”**

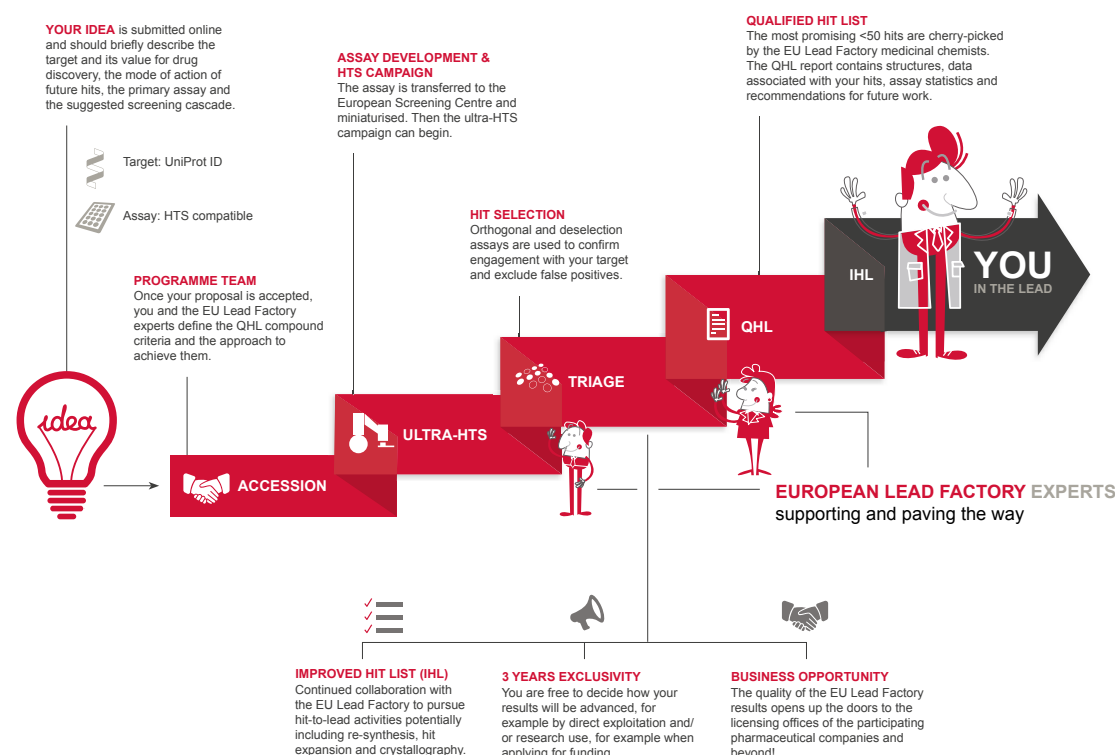
**Dr Mike Rawling**  
Senior Scientist Proximagen Ltd, Cambridge, UK

<sup>6</sup> Expansion of chemical space for collaborative lead generation and drug discovery – the European Lead Factory Perspective, A. Karawajczyk, F. Giordanetto, J. Benninghof, D. Hamza, T. Kalliokoski, K. Pouwer, R. Morgentin, A. Nelson, G. Müller, A. Piechot, D. Tzalis, Drug Discovery Today 20 (11), 1310–1316 doi: 10.1016/j.drudis.2015.09.009  
<sup>7</sup> Mullard A. 2015 FDA drug approvals. Nat Rev Drug Discov (2016) 15(2):73–6.

## 1.3 SUMMARY OF PROGRESS

*In just five years, the European Lead Factory has started up, shown it works and realized first successes more efficiently than anticipated*

In 2013, the immediate access to the industry compounds gave the project a flying start. In just six months, over 320,000 compounds were cherry-picked from seven pharmaceutical companies, reformatted and plated to form the core of the Joint European Compound Library. The crowdsourcing of innovative drug targets and library ideas also kicked off in the first half year and managed to attract innovative and technically mature programmes from European academia and SMEs. The facilities of the European Screening Centre were rapidly made available. As a result, the first uHTS for a crowdsourced drug discovery programme was accomplished already in August 2013, the first set of new compounds added by March 2014, and the first qualified hit list delivered in May 2014. To date, 161 QHLs and 37 IHLs have been completed and the final 30 EFPIA programmes will be completed within the respective organizations during the post-term period.



**Figure 4.** The execution of a crowdsourced target programme.

*Any researcher, any target, any disease*

In these five years, ELF has shown it works. Any European researcher from academia or a small and medium-sized enterprise has been able to submit proposals to use the JECL for screening through the European Screening Centre (see Figure 4). Drug targets of all types and in all therapeutic areas are submitted. Through a thorough triaging process of the primary hits, up to 50 most promising drug discovery molecules can be delivered. After a three-year period, in which further IP may be generated, the results of the public programmes are disseminated. Within the project, crowdsourcing provides not only a constant flow of innovation but also new opportunities for collaborations between academic groups, SMEs and EFPIA members on both scientific and commercial grounds.



*More efficiently than anticipated*

The original plan aimed at crowdsourcing 120 programmes and estimated 20% attrition in assay development before screening. In practice, by establishing a critical review and selection process attrition was reduced later in the process. Discussions to initiating programmes were conducted with 200+ target owners, which yielded 157 full proposals. Of those 88 were selected and 72 resulted in QHLs. By focussing on quality, 50% (37) of those programmes could receive highly valued medicinal chemistry support and progress to the improved hit list (IHL) stage. In the end, 109 hit list reports (QHL + IHL) were delivered to programme owners at European biotech SMEs and academia. Over time, the ELF partners learned to speed up their processes. This is illustrated by the remarkable output in the last 18 months: 21 uHTS campaigns completed, 36 (50%) QHL and 23 (64%) IHL reports delivered.

*Flexibility to ensure results*

The European Lead Factory has made small adjustments to maximise the output and impact. Midway through the project, the project agreement was adapted to attract more programmes addressing neglected tropical diseases. Waiving clinical or diagnostic milestone payments freed charities and other organizations from financial obligations in their pursuit of new therapies for patients in the least developed countries. As a result, 25% of the crowdsourced ELF portfolio today addresses infectious diseases of less commercial value, yet of considerable societal importance. To give more crowdsourced programmes a chance to conclude screening activities, deliver all pending QHLs, and complete the library enhancement programme, the ELF project term was extended by five months. In this period alone, 18,000 novel compounds were added to JECL and 19 QHL and 13 IHL reports were delivered to programme owners. In addition, programme plans and detailed protocols for uHTS-ready assays were delivered to programmes that did not develop in time to progress to uHTS. These have proved useful for example in grant applications.

## 1.4 SIGNIFICANT ACHIEVEMENTS

*The European Lead Factory can present success stories that demonstrate its potential to accelerate drug discovery in general and for societal priorities in particular*

More than 50 academic organisations and young biotech companies have already benefitted from a very significant kick-start to their 72 drug discovery programmes. In addition, the prospect of owning intellectual property rights creates many opportunities for further funding and business development. We have selected five case studies to illustrate the potential and relevance of the ELF drug discovery platform.

**Oncology:** The research focus of Reuven Stein (University of Tel Aviv) is the tumour microenvironment. He has discovered a protein that plays an essential role in tumour progression in cancers such as glioma and melanoma. After failing to find tractable and attractive hits in a smallscale screen for inhibitors in-house, they successfully applied to the European Lead Factory. The screen performed by the ELF scientists resulted in a Qualified Hit List of 50 compounds that “exceeded all expectations. The list included several compound classes of unprecedented potency with low nanomolar activities not only on the target itself, but also in the cell-based assay”.

Medicinal chemistry professor Micha Fridman adds: “The compounds have the inhibition levels and physicochemical properties you would expect from an Active Pharmaceutical Ingredient.” In another oncology programme, a candidate drug has been nominated and a partnering deal has been closed with a party that can develop it further towards the clinic.



**“Quality in early drug discovery is an investment later returned as benefit for the patient.”**

**James Duffy**  
Medicines for Malaria Venture

**Metabolic disease:** For Margit Mahlapuu (University of Gothenburg and spin-out ScandiCure), “the collaboration with ELF provided the missing piece in the puzzle”. She had identified a new target which could be used to reverse metabolic complications in type 2 diabetes, but she lacked the chemistry resources and the national screening platform failed to deliver tractable hits. She applied to ELF, which provided her with potent and selective compounds. They enabled pharmaceutical validation of the target and provided an excellent starting point for further development towards the clinic. Based on this, Mahlapuu successfully created the spin-out company ScandiCure which recently announced a partnering deal with Servier, an international pharmaceutical company.

**Parkinson’s disease and motor degenerative disease:** Although a lot of research has been directed towards these diseases, they remain incurable. Richard Mead (University of Sheffield and spin-out Keapstone Therapeutics) works with a challenging protein-protein interaction target and a disease area that requires the future drug molecules to penetrate the blood–brain barrier. “Many, including ourselves, have screened various commercial and academic libraries, but never found anything useful. The diversity and quality of the Joint European Compound Library is not available anywhere else.” In an unprecedented collaboration, Parkinson’s UK and the University of Sheffield have launched a joint venture biotech company, Keapstone Therapeutics, to progress the ELF hits. Parkinson’s UK has allocated 1.3 billion GBP (1.5M€) to further develop compounds that boost the internal cellular defence mechanisms against oxidative stress. Dr Mead confirmed the pivotal role of the European Lead Factory: “It would have been absolutely impossible without the high-quality work that the European Lead Factory provided. From assisting with protein production, the optimisation of the HTS assay, developing a totally new biophysical assay, the hit expansion and medicinal chemistry, new protein constructs, and finally also solving inhibitor-bound protein crystal structures.”

**Antimicrobial resistance:** The University of Oxford takes the next step in targeting antimicrobial resistance with help of the results and hit compounds delivered by the European Lead Factory. The Oxford team, led by Professor Chris Schofield, collaborates with IMI’s European Gram-Negative Antibacterial Engine (ENABLE) project to further progress this programme towards clinical development. So far, it is the only academic programme to survive the ENABLE’s stringent attrition criteria. Professor Schofield stresses the importance of the European Lead Factory in “transforming an almost impossible task for an individual academic group into a solid scientific and commercially viable pathway.”

**Neglected tropical diseases:** With globalisation and climate change many diseases traditionally associated with remote and poor parts of the world pose a real threat to all the world’s population. One example is leishmaniasis, the most severe form of which (visceral leishmaniasis) is fatal if left untreated. Professor Anabela Cordeiro-da-Silva, principal investigator at i3S in Portugal is “...very excited that the European Lead Factory has dedicated resources to our research programme targeting leishmaniasis. With this project, we have found the most effective and selective inhibitors known to date of this parasite enzyme. It provides real hope to develop a successful treatment for leishmaniasis.”

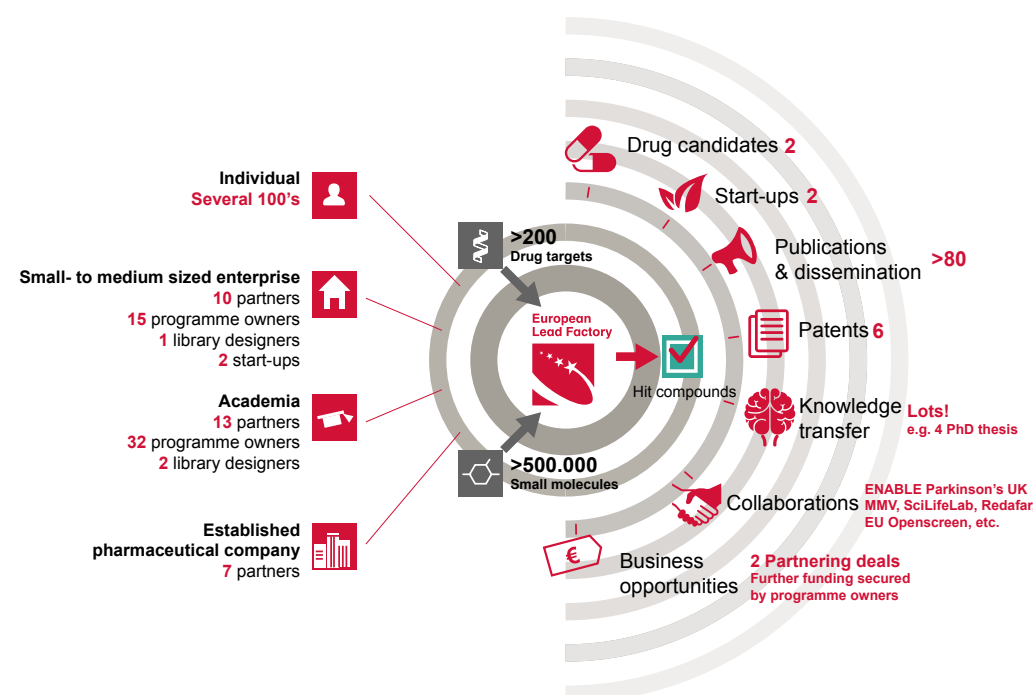
These case studies have helped promote the value of the ELF platform across Europe and attract prospective programme owners and new partners for the follow-up project ESCulab, such as the Medicines for Malaria Venture.



## 1.5 SCIENTIFIC AND TECHNICAL RESULTS/FOREGROUNDS OF THE PROJECT

*In addition to drug discovery starting points, the European Lead Factory delivers publicly available insights and infrastructure, and collective intelligence*

The European Lead Factory's success is designing and synthesizing novel compounds, crowdsourcing targets, screening and producing qualified and improved hit lists has been described in the preceding sections. But ELF delivers more results to its participants, the broader scientific community and society (see Figure 5). In this section we briefly summarize all results (as of June 2018) and elaborate on those not previously mentioned.<sup>8</sup>



**Figure 5.** An overview of ELF interactions, output, results and impact.



## DIRECT PROJECT RESULTS

- Joint European Compound Library (JECL) with >500,000 small molecules (320,000 contributed by industry and >200,000 synthesized in the project).
- 72 qualified and 37 improved hit lists from crowdsourcing programmes delivered to target owners
- 30% follow-up work on pharmaceutical partners screens (29 of 89)
- 2 drug candidates
- 3 industry drug discovery programmes in lead optimization phase
- 5,649 qualified hits in total delivered to public (2,406) and private target owners (3,243)
- >3,000 bespoke compounds synthesised in the hit validation and hit-to-lead phase of crowdsourced target programmes; >40 crystals structures of target-compound complexes solved; >280 bespoke assays developed to extract the most interesting hits for crowdsourced programmes<sup>9</sup>
- 3 bespoke IT systems (see below)

## LANDMARK ACHIEVEMENTS

- 5 patents on ELF compounds for treatment of multi-resistant bacteria infections, pain and cancer
- 2 partnering deals: one between ScandiCure AB and Servier (for metabolic diseases, see page 14) and another yet to be publicly announced
- 1 virtual biotech with 1.3 M£ million GBP (1.5 M€) in funding Keapstone Therapeutics, addressing Parkinson's disease, see page 15)
- 1 ELF preclinical development programme funded by IMI's ENABLE (see page 15)
- In vivo proof-of-concept generated with ELF compounds

<sup>8</sup> For more information, please visit the ELF website [www.europeanleadfactory.eu](http://www.europeanleadfactory.eu)  
<sup>9</sup> Jones et al FutMedChem, 2015, 1847



## DISSEMINATION AND KNOWLEDGE EXCHANGE

- Close to 90 scientific, peer-reviewed scientific articles
- 4 PhD theses enhanced with ELF target programme assay development and screening results
- >100 academic postdoctoral fellows trained in industry methods and approaches

## INFORMATION TECHNOLOGY AND DATA MANAGEMENT

The European Lead Factory developed three bespoke IT systems:

- Honest Data Broker (HDB), developed jointly by the University of Dundee and subcontractor Biovia, is a high capacity database that can be efficiently interrogated using state-of-the-art scientific tools whilst ensuring detailed business rules on data security are rigorously enforced<sup>10</sup>. Besides the data management required for hit triaging to generate qualified and improved hit lists, the HDB also stores cross-programme information on over 200 target programmes and 161 QHLs that can be exploited to inform future screening campaigns. The system has demonstrated its technical capabilities and secured the confidence of all partners, particularly the pharmaceutical industry, making it the tool of choice for follow-up activities, such as the proposed IMI2 ESCulab project. For its achievements, the HDB received the BioIT World: Knowledge Management Award in 2015.
- ChemAxon developed a web-based tool that facilitates the submission, review and selection of the library proposals. The tool was designed to support all stages of library proposal development, submission, review and selection. Data of submitted proposals has been archived. Proposals that have been selected and undergone validation of feasibility were moved to TarosGate. Library proposals that could not be validated will not be exploited further. The submitting party maintains any rights associated with the proposal.

<sup>10</sup> Paillard et al, The ELF Honest Data Broker: informatics enabling public-private collaboration in a precompetitive arena. Drug Discovery Today 21(1), 2016, 97



- TarosGate (to be used under Microsoft Windows, MacOS and Linux) is a chemistry workflow management system with a secure built-in electronic laboratory notebook. Specifically developed for ELF, it combines four important aspects of the collaborative synthesis work: i) documentation, ii) project management, iii) communication and iv) compound logistics for shipment of newly synthesized library compounds. It provides a stable, secure platform for data collection of a daily work in synthetic chemical laboratories, monitoring of project progress and resource management.

### Collective Intelligence

The Joint European Compound Library, the ELF IT systems and the European Screening Centre are the main assets of ELF. But the keys to ELF's success are the experts across the consortium who understand how to execute and interpret data and share experiences, the support office that enables knowledge exchange and the management continuously fine-tuning the operations. ELF is true partnership and it is the people who make it work. ELF is powered by collective intelligence.

## 1.6 POTENTIAL IMPACT AND MAIN DISSEMINATION ACTIVITIES AND EXPLOITATION OF RESULTS

*The European Lead Factory has shown it can deliver health and wealth for society, make open innovation work and boost science*

The European Lead Factory established a collaborative model of drug discovery that helped improve the efficiency and productivity of developing new medicines for unmet medical needs (see Figure 6). It has demonstrated that it can deliver hit compounds highly suitable for further development, collective intelligence that capitalizes on previous investment, and investable programs, scalable (new) SMEs and sustained corporate R&D in Europe. ELF is an excellent example of open innovation that works mutually and that truly exchanges and enhances knowledge between academia and industry.

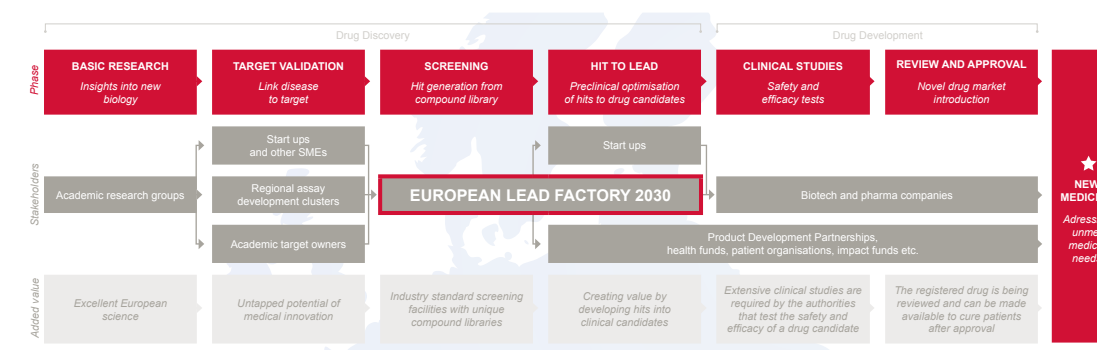


Figure 6. The European Lead Factory in the medicine research landscape, today and tomorrow.

### *More promising drug candidates*

By crowdsourcing targets and screening targets against its large, high-quality compound collection, the European Lead Factory helps identifying more promising drug candidates. Over the years, ELF has built a balanced portfolio of uniquely diverse drug discovery programmes. Irrespective of factors such as commercial potential, alignment with an industry-specific therapeutic focus and shareholder preferences, the selection criteria were based on novelty, scientific excellence and innovation potential. Some of these were orphan targets, with only genetic data supporting their relevance. Some were owned by academic researchers, who would not otherwise have had a chance to screen them, and surely not on this scale. Other programmes had hit a roadblock at the individual partner that were now given access to a broader compound library than would otherwise be available to them. Thanks to the European Lead Factory, such roadblocks could be overcome, and more projects progressed. Over time, these should yield more drug discovery programmes and ultimately lead to new medicines that benefit patients. If delivered by European (divisions of) corporates and SMEs, they increase both the health and wealth of our society.

### *Unlocking untapped medical innovation that capitalizes on previous public and private investments*

The European Lead Factory combines the experience of big pharmaceutical companies with the agility of SMEs and the innovation in academia. It uses this collective intelligence to unlock an untapped potential of medical innovations – without it, many targets identified by academic researchers or SMEs would go unscreened and the high-quality chemical compounds in corporate libraries underused (let alone expanded with novel compounds in a library open to all). It stands to reason that tapping into this potential would increase the number of relevant hits (i.e. efficiency) and leverage earlier investments made through public funding of fundamental research and private investments in high quality chemical matter. Moreover, there are first indications that ELF is indeed able to unlock those opportunities that none of the partners alone would be able to seize.

### *Investable programmes, scalable (new) SMEs and corporate R&D in Europe*

In addition to leveraging earlier investments in chemistry and biology, further economic activity benefits Europe. ELF produces investable programmes to develop ELF hits or leads into clinical candidates. Corporate partners will produce and run these programmes themselves, in-house. But academic groups, SMEs and charities and foundations (e.g. Medicines for Malaria Venture) now also have that opportunity. This might lead to more ventures and/or new business lines in existing companies that can attract funding and scale into viable, growing, European SMEs. ELF thus strengthens the European research infrastructure and increases the competitiveness of its European academic, SME and industry partners.



“ELF really helped us to kick-start the company. For (starting) SMEs it is often difficult to get new clients to work for. They want to know what you have achieved and want proof that you have the capability to execute the project. With ELF we have been able to run a lot of screens, which gave us a strong track record.”

Dr Steven van Helden  
Chief Technical Officer, Pivot Park Screening Centre

### *Open innovation made practical and productive*

Open innovation is a much-touted term and much-promising idea – if you can make it work.

In practise, using “external ideas as well as internal ideas, and internal and external paths to market, as (...) firms look to advance their technology”<sup>11</sup> is far from straightforward. Pre-competitive R&D collaborations between academia, corporates and SMEs have been successfully set up, but individual projects within these programs mostly involve just one corporate partner and a single SME.

The competitive implications of sharing even just knowledge or background IP are hard to manage. The European Lead Factory is exceptional because its partners share proprietary knowledge not just with academia or SMEs that they could contract work to, but with direct competitors. The Joint European Compound Library really is a shared resource that directly boosts the productivity of each partner’s drug discovery. Crowdsourcing also creates many more opportunities for them to enrich their pipelines through partnering or acquisition of hit lists, programmes or ventures. The European Lead actory has shown it can operate at the pre-competitive/competitive interface and make open innovation practical and productive for industry and academia together.

### *A boost for science*

An unusual feature of the European Lead Factory is that it facilitates “bi-directional” exchange as well as co-creation and translation of innovative ideas. Knowledge does not just flow from academia to industry but in the other direction, as well. The Joint European Compound Library, building on years of research in both industry and academia, is a prime example. It not only supports drug discovery but helps open new avenues of biological and chemical research.

In the few years it has been operational, the European Lead Factory has already induced over 80 peer-reviewed scientific publications, in addition to numerous conference proceedings and posters. New methodologies in chemistry, and biochemical and biophysical assays techniques have been developed and applied. Public dissemination of these innovations will benefit the scientific community worldwide.

ELF provides participating scientists, particularly those at an early stage of their career, with a unique working environment and opportunities to collaborate across the boundaries of academia, SMEs and corporates, and see their work have real and immediate impact. An example is the work in the chemistry consortium, where innovative library ideas were developed by academics and SMEs and translated into screening compounds that meet industrial standards of quality and scalable production. It successfully aligned chemical synthesis with drug discovery needs, and the introduced methods have been taken up by the chemistry community. Researchers involved have achieved prominent positions in industry or academia, scholarships and awards based on their experience gained in ELF (e.g. 2018 EFMC UCB-Ehrlich award for Prof. Adam Nelson<sup>12</sup> and Dutch Prix Galien for Prof. Mario van der Stelt<sup>13</sup>). Overall, more than 100 academic postdoctoral fellows have been trained in industry methods and approaches, increasing their competitiveness for the European job market.

<sup>11</sup>Chesbrough, Henry William (March 2003). Open Innovation: The new imperative for creating and profiting from technology. Boston: Harvard Business School Press

<sup>12</sup> <https://www.europeanleadfactory.eu/node/274>

<sup>13</sup> <https://www.europeanleadfactory.eu/node/214>



## 1.7 LESSONS LEARNED AND FURTHER OPPORTUNITIES FOR RESEARCH

### *The European Lead Factory is a blueprint for public-private partnerships*

The European Lead Factory has successfully established the assets, working practices and tools for true collaborative innovation by a consortium of public and private partners. In many ways, ELF and its partners were pioneers: compound sharing, crowdsourcing innovation in biology and chemistry, partnering opportunities offered to several competitors at once, and a legal framework that allows value generation for both direct and indirect beneficiaries.

In an unprecedented step, pharmaceutical companies took the initiative to open their “treasure chests” for public use and cede control over the process to an independent third party. The compound libraries they contributed are a key component of their innovation power. That they are prepared to share this knowledge with direct competitors reflects not only the value they see in ELF but the trust they have in its ability to safeguard the individual interests of all partners.

ELF and its partners developed innovative working practices and tools to balance effective execution and knowledge exchange with intellectual property (IP) protection. The European Screening Centre was set up to screen, triage and progress crowdsourced drug discovery programmes in a setting that was industry-standard, but independent. The Honest Data Broker (HDB), the digital heart of the ELF operations, allowed effective yet anonymous tracing of compounds and screening data, fine-grained access rights, and a fast ordering process for compounds to confirm biological activity, perform more detailed kinetic characterisations or check compound purity. The HDB also performed a key role in linking ELF partners and coordinating their efforts. Over the course of the project, the consortium has further optimized its workflows and adapted to recent developments in the science community.

For all the value the European Lead Factory has for its private partners, the main value proposition of the project remains its public interest focus. It addresses a public need, it is in part publicly funded, and its public-private nature governed by an independent trusted third party is what helps safeguard all interests and make it work.



**“The European Lead Factory provides a structure necessary to fill the gap in Drug Discovery research between academia, industry and society”**

Michael Tadros  
Fundación Botín, Spain

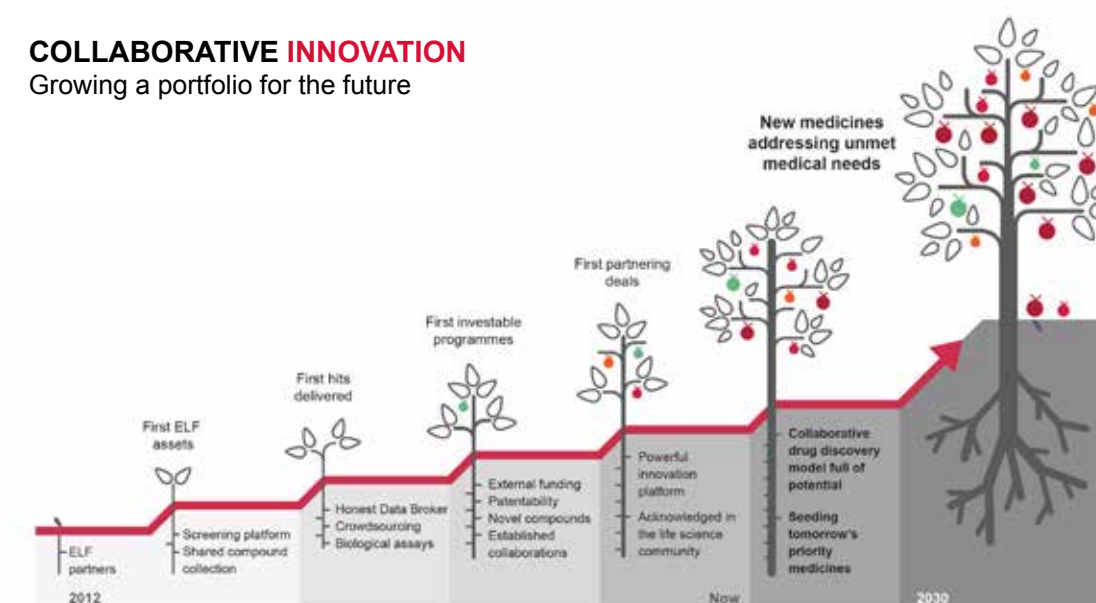
The most valuable lessons learned in setting up and operating the European Lead Factory are that and how public-private partnerships can be made to work and deliver results. This makes ELF a blueprint for (future) partnerships, such as the new IMI2 call ESCulab, and its assets, processes, tools, network and experience can be used to kick-start new initiatives.

### *Seeding tomorrow's priority medicines*

Establishing the European Lead Factory was a first step. We have only just started to unlock its full potential (see Figure 7). In the past five years, we formed a consortium, created trust, established a first compound collection, started crowdsourcing targets and chemistry, initiated screening and the delivery of hits, developed the first investable programmes, and struck the first partnering deals. In the timelines of drug discovery and development, five years is just enough to demonstrate ELF's potential as a viable and valuable catalyst. The Joint European Compound Library and the European Screening Centre are assets that appreciate with use: every new partner and project adds targets and/or compounds that contributes to more diverse and better hits. ELF has positioned itself at the centre of collaborative drug discovery for tomorrow's priority medicines. Its role and function within the ecosystem are widely acknowledged and exemplified by the close collaboration with complementary national and international drug discovery communities. The demand for ELF's services continues to grow as the first success stories are being presented. In summary: ELF has pioneered a model of collaborative drug discovery that already delivers results and holds considerable further potential. It is both a blueprint for new public-private partnerships and a successful collaboration that should be extended and expanded to capitalize on the investments made and continue leading the way to new medicines for unmet medical needs.

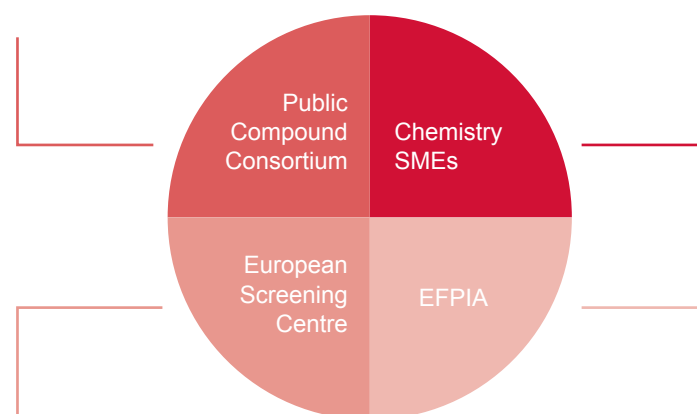
### COLLABORATIVE INNOVATION

Growing a portfolio for the future



**Figure 7.** The European Lead Factory is already bearing fruit and is teeming with potential.

# THE EUROPEAN LEAD FACTORY, MADE POSSIBLE THROUGH



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