

Stakeholder Meeting showcases the continuing Success of the European Lead Factory

On 13 November 2019, the first Stakeholder Meeting of the European Lead Factory (ELF) under the new ESCulab-funding provided a lively forum for participants to share their future goals and stories of success. Many of the partners present gave updates on how screens made by ELF have resulted in promising leads for novel drugs. The management of ELF outlined an ambitious vision for the future, including the fact that charities will soon be invited to screen interesting targets of their choice.

The ELF Stakeholder Meeting took place at the headquarters of Merck in Darmstadt (Germany) and brought together a diverse group of drug discovery experts from charities, academia and industry. With the newly rewarded budget of €36.5 million under the second framework of the Innovative Medicines Initiative (IMI) for ESCulab (European Screening Centre: unique library for attractive biology), ELF has entered into its second phase. For the next five years, ELF will initiate 185 new drug discovery projects by screening medically relevant drug targets from European researchers, small- and medium-sized enterprises, and the pharmaceutical industry against the ELF library of 535,000 unique chemical compounds. In addition to target-based screens, ELF now also offers phenotypic screens, including High Content Screens. Along with Grünenthal and Servier, ELF also welcomes the Medicines for Malaria Venture (MMV) to the new consortium.

Overall, the Stakeholder Meeting provided a solid platform for showcasing the many successful drug discovery programmes that have originated from ELF.

“ELF’s innovative compound collection enabled us to identify chemical matter for two new programmes superior to our internal and superior to commercial screening collections.”

Hubert Haag (Sanofi: Director Technology Platforms - Global Business Development & Licensing)

Peter Halle (SVP, Head of External Innovation and Head of the Translational Innovation Platform Immuno-Oncology at Merck) explained the concept of open innovation at Merck and how the company participates in ELF in a pre-competitive manner to pool resources and expertise. High-throughput screening is a core technology at Merck. Out of the 20 screens in eight target classes performed at ELF, 10 projects have advanced to subsequent phases.

Hugh Lavery (Head of Scientific Operations, Innovative Medicines Initiative) outlined the future of public-private partnerships in health in the European arena. Lavery provided an insight into the new Horizon Europe framework, clearly stating that discussions are in full swing in Brussels around the successor of Horizon 2020 and IMI. A stronger focus on general healthcare and less emphasis on so-called ‘wetlab’ research seems to be the direction in which Horizon Europe is moving. Lavery encouraged all participants to share their views in the upcoming consultation that ended in November 2019.

Stefan Jaroch (Head External Innovation Technologies, Bayer) together with **Jon de Vlieger** (Director Business Development, Lygature) looked back at what has been achieved in the first phase of ELF. A phenomenal 191 targets have been screened and the public compound library has been expanded by close to 200,000 molecules resulting in 7,500 hits reported back to target owners. The inception of the Keapstone

Therapeutics by Sheffield University and further funding through Parkinson UK or the Swedish company Scandicure who develop drugs for type 2 diabetes, now in collaboration with Servier, are just two of the many real-world examples of our way of collaborative drug discovery. The future of ELF holds much in store as the project opens its doors for paid screens from charities.

Dirk Finsinger (Director Medicinal, Early Pipeline Technologies, Merck) and **Dimitrios Tzalis** (CEO Taros) presented the evolution of the ELF compound library. The library now contains the full public compound collection (PCC) generated during ELF1, which nicely complements the compounds sourced from our industrial partners. The updated library consists of many novel scaffolds of which 40% are new. The overall quality of the ELF library has substantially increased over the years, as shown by several measures like Fsp³ content /chiral atom count.

Per Arvidsson (Platform Director Drug Discovery & Development Platform, SciLifeLab) strongly advocated how regional hubs strengthen European collaborative drug discovery. This Swedish venture was tasked with turning academic discoveries into innovations. For the past five years, SciLifeLab has built up a national infrastructure for Drug Discovery & Development. With a smart fit for the capabilities of ELF, SciLifeLab has delivered multiple high-quality drug discovery programmes that are globally competitive for funding and clinical development.

Volkhart Li (Alliance Manager, Bayer) showcased the success stories from the EFPIA Partners (European Federation of Pharmaceutical Industries and Associations). Li stressed, in an inspirational way, the value of non-tangible aspects such as courage, curiosity, commitment and trust. The impact of ELF was made clear by the quotes from the EFPIA Partners, which are highlighted throughout this report. For Bayer itself, screening the ELF library delivered attractive chemical solutions in two cases.

“ELF did not only accelerate an important hit to lead decision for one of our programmes, but also identified two novel hits for an interesting target, leading to the idea to design a new hybrid molecule.”

Dirk Finsinger (Merck: Director Medicinal Chemistry, Innovation & Externalization)

“Malaria takes the life of a child every two minutes”, was how **James Duffy** (Director Drug Discovery, MMV) expressed the urgent need for new antimalarial drugs to ultimately eradicate this terrible disease. MMV finds and develops novel drug candidates through many strong collaborations exploring different avenues such as long acting injectable antimalarial drugs for prophylaxis. As an associate EFPIA-member of ELF, MMV is looking forward to the results of the five screens of the ESCulab library that will be carried out during the 5-year project. Duffy further highlighted the impact of the compound libraries that MMV have made available at no cost for researchers working on infectious and neglected diseases.

Christopher Cooper (Senior Director Chemistry, TB Alliance) described the current Tuberculosis (TB) pandemic. TB is the leading infectious disease killer, currently responsible for 1.6 million deaths. With 300,000 co-morbidities, TB is the leading cause of death for HIV/Aids patients. The current therapy takes 6-18+ months, can exceed 14,000 pills for drug-resistant strains and can cost more than \$10,000 per treatment. The danger of drug-resistant TB looms large. The TB Alliance leverages its experiences in developing novel drugs by having a strong pipeline of new treatments in place. The organisation is part of the TB Drug Accelerator, an innovative partnership aimed at optimising TB drug discovery.

Gang Liu (Senior Program Officer, Bill & Melinda Gates Foundation) outlined the efforts of the Bill & Melinda Gates Foundation to address global public health issues. More specifically, Liu discussed the priorities of the foundation in drug discovery and outlined many of the foundation's approaches and strategic partnerships. With a clear interest in piloting emerging (unproven) technologies and applications of artificial intelligence, the foundation aims to access novel chemical entities. Liu finished his talk with the statement: "The work is complicated. Why we do it is not."

Achim Schnauffer (Professor in Parasite and Mitochondrial Biology, University of Edinburgh) gave a detailed talk on trypanosomatid parasites – a class of parasites primarily transmitted by insects and the cause of several neglected diseases such as leishmaniasis and sleeping sickness. Remarkable properties of the kinetoplastid parasite are the dense DNA-containing granule within the cell's single mitochondrion, and the RNA editing process required to express the encoded genes. Through an ELF programme, the targeting of ligase REL1, a key part of the RNA editing core complex, has delivered chemically diverse small molecule inhibitors, some of which inhibit REL1 from several trypanosomatid species.

"We are delighted to see that the ELF compound library could add complementary value to our own high-quality in-house compound collection. Despite its considerably smaller size, we have seen encouraging results that exceeded our expectations, particularly with very low druggable targets. Notably, screening the ELF library delivered attractive chemical matter in two cases and made an ELF hit series the starting point for a front runner project in our competitive portfolio. In addition, the ELF's crowd sourcing of attractive biology enabled us to engage with one applicant to negotiate a potential bilateral collaboration in the field of target biology. Overall, we experienced that ELF can (indeed) make a difference."

Volkhart Li (Bayer AG: Alliance Manager)

Hugo Ceulemans (Scientific Director Discovery Data Sciences, Janssen) wants to use artificial intelligence to select the best drug candidates by predicting activities from the 10^{60} drug-like small molecules. To put this number into perspective, it is estimated that planet earth contains 10^{20} grains of sand! The IMI-project MELLODDY combines federated learning with blockchain technology and machine learning across databases of EFPIA Partners in a privacy-preserving manner to improve each partner's activity prediction models. Ceulemans was able to convey to the audience that they are already witnessing the future of drug discovery.

Ton Rijnders (Scientific Director, Lygature) closed the session with a look to the future. Rijnders envisioned a major expansion of ELF over the next 12 years to 2030. It is necessary to further expand screening activities towards new targets and personalised cell lines and broaden the activities of ELF to include hit-to-lead development. This approach will maximise the chances of programmes being partnered or supported by private investment, thus increasing their value until they have the potential to be primed for drug development. With the many success stories that were presented by the different ELF Partners and the strong unmet patient need for innovative drugs in many disease areas, the future of ELF looks bright.

If you would like to learn more about the European Lead Factory and how it can supercharge your research on interesting disease biology, please contact the Program Office by email at: programme@europeanleadfactory.eu or check out our website: www.europeanleadfactory.eu.

More partner testimonials can be found here: <https://www.europeanleadfactory.eu/results/testimonials>