D1.5 Enhanced Business Plan and financial sustainability model based on EU-OPENSCREEN-DRIVE outcomes

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1 Introduction

EU-OPENSCREEN is the European Research Infrastructure (RI) which supports scientists in the development of novel chemical compounds that elicit specific biological responses in organisms, cells, or cellular components in a specific and well characterised manner. These chemical compounds can be used by scientists as research tools ('chemical probes') to study fundamental cellular processes (e.g., signalling or metabolic pathways in immune responses, tissue repair, etc.) or as early drug leads which can be progressed into medicines. EU-OPENSCREEN screens collections of over 100,000 compounds using automated robotics-based high-throughput screening platforms, and the identified chemical probes are subsequently developed using hit-to-probe optimisation.

The mission of EU-OPENSCREEN includes the following actions:

- Accelerating the discovery of biologically active substances in all areas of the life sciences;
- Facilitating transnational access to the most advanced technologies, chemical and biological resources, knowledge, and expertise;
- Advancing knowledge of the molecular mechanisms underlying complex biological processes;
- Increasing knowledge on the bioactivities of chemical substances as well as the responses of biological systems to these substances; and
- Promoting the availability of safe and efficacious chemical products for unmet needs.

EU-OPENSCREEN was established as a European Research Infrastructure Consortium (ERIC) in April 2018 by the following seven ERIC member countries ('members'): the Czech Republic, Germany, Finland, Latvia, Norway, Poland, and Spain, with Denmark participating as an observer country. Currently, the EU-OPENSCREEN ERIC is supported by 10 members, including Denmark, Portugal, and Sweden. The founding member countries committed to supporting the EU-OPENSCREEN ERIC for at least five years; now that these initial five years have passed, countries are now eligible to withdraw their support. Additional countries may also join the EU-OPENSCREEN ERIC as new members or observers.

This document describes the scientific and organisational concept for the EU-OPENSCREEN ERIC for the next five years (2024–2028). This concept builds on the results of the DRIVE project and takes into consideration other ongoing and soon-to-be-launched Horizon Europe projects which have been selected for funding.

2 Scientific plan for 2024-2028

2.1 Current partner sites

EU-OPENSCREEN is a distributed RI with local partner sites in its 10 member countries. Portugal and Sweden joined as new member countries in 2022, and new partner sites in these two countries were included as local partner sites within EU-OPENSCREEN. The partner sites implement EU-OPENSCREEN's scientific user projects and participate in various EU-OPENSCREEN-led Horizon 2020 and Horizon Europe projects. Selected partner sites implement the bioprofiling activities, which are described in more detail below, and organise training activities.

Member countries may also nominate additional partner sites. The partner site selection procedure consists of three steps: (i) nomination of a potential partner site by its host country,

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which must be an EU-OPENSCREEN ERIC member country; (ii) external evaluation of the nominated site in terms of scientific excellence and technical capabilities; and (iii) approval of the positively evaluated site by the Assembly of Members (AoM).

Currently, there are three distinct partner site categories defined within EU-OPENSCREEN:

Screening Partner Sites:

Screening partner sites offer users access to assay adaptation services and automated technologies to allow for large-scale 100,000-compound screening campaigns across a wide range of formats, including biochemical, cell-based, and model organism-based screens. Specialist screening sites complement larger high-capacity screening sites by offering specialised expertise and technologies that are not commonly available at the high-capacity screening facilities (e.g., BSL3 capacities). All screening sites adhere to high-quality operating standards.

Chemistry Partner Sites:

Hit-to-tool and hit-to-lead optimisation user projects are carried out at EU-OPENSCREEN chemistry partner sites. All chemistry partner sites have demonstrable expertise in chemical biology and/or medicinal chemistry. Their capabilities cover general medicinal and synthetic chemistry activities such as SAR determination, compound design, synthesis, analytics, and structural confirmation. Chemistry partner sites may also be closely associated with or located in the same host institution as a screening partner site; for example, the Leibniz Institute for Molecular Pharmacology in Berlin, Germany, and the Karolinska Institute in Sweden each co-host two partner sites, one for screening and one for chemistry.

Database Hosting Site:

The screening and chemistry partner sites provide chemical biology-related services and generate substantial amounts of data covering a variety of chemicals, proteins, assays, screens, and chemical optimisation programs. Relevant data from external user projects and internal activities (e.g., compound quality control and bioprofiling) are collected, stored, annotated, and made available in EU-OPENSCREEN's large-scale open-access European Chemical Biology Database (ECBD;), hosted by our partner site, the Institute of Molecular Genetics (IMG), in Prague, Czech Republic. The team is responsible for designing, creating, and hosting the ECBD.

Currently, EU-OPENSCREEN has 22 screening partner sites, 11 chemistry partner sites, and one database host. The number of partner sites are balanced between the different countries: all countries host at least one partner site, and no country has more than five partner sites. A list of all partner sites is available on the EU-OPENSCREEN website (). All partner sites are profiled in detail in EU-OPENSCREEN's partner site brochure (), which is currently being updated.

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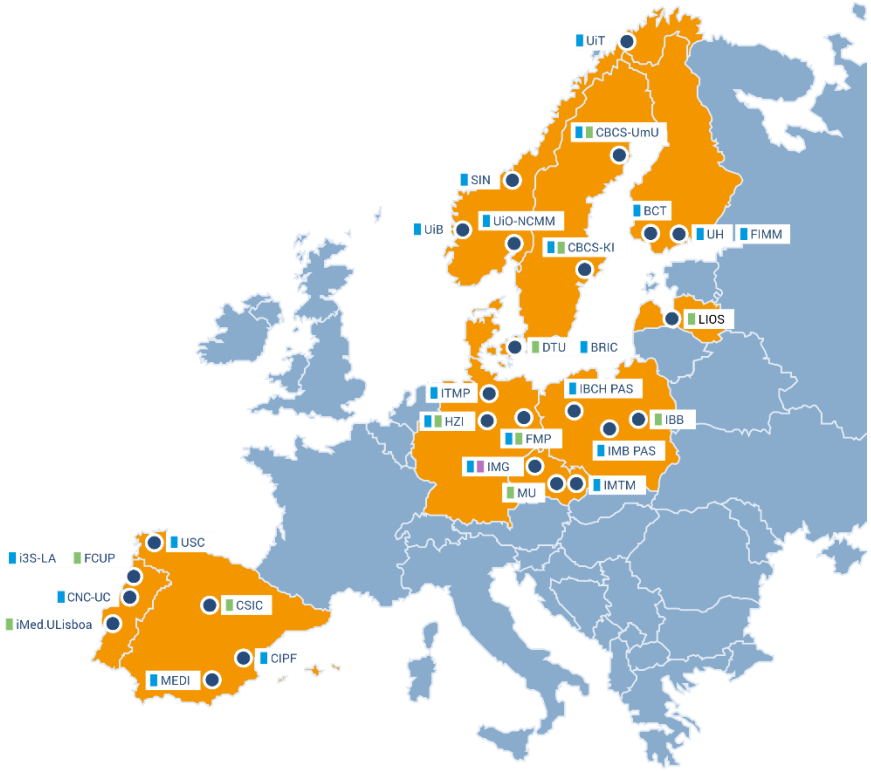

Figure 1: Map of the EU-OPENSCREEN ERIC member countries and partner sites (as of October 2023).

2.2 New partner sites

In 2024, a new partner site category will be launched for the implementation of chemoproteomics and for compound disposition studies. The handbook for this partner site category is available, and the AoM has agreed to nominate, evaluate, and select the first chemoproteomics partner sites in 2024. Importantly, the successful implementation of chemoproteomics studies typically requires the involvement of two or more EU-OPENSCREEN sites in order to achieve full technical coverage of all necessary experimental and analysis activities. The chemoproteomics sites will therefore offer a subset of services that can be combined with the offerings of other EU-OPENSCREEN chemoproteomics sites (with coordination and support from the EU-OPENSCREEN Central Office) to realise a comprehensive user service solution.

2.3 Current services

Out of 50 new medical entities (NMEs) approved in 2021, 72% were small molecule-based therapeutics – the main focus of EU-OPENSCREEN's research. Compound screening and medicinal chemistry has made indispensable contributions to the development of these drugs. Access to the required technologies, expertise, and resources, however, is often not readily available to many scientists.

EU-OPENSCREEN therefore plays a significant role in the European research landscape as a pan-European 'ESFRI Landmark' project dedicated to accelerating the discovery of new chemical probes and drugs by providing researchers in academia and industry across Europe and worldwide access to state-of-the-art high-throughput screening (HTS) platforms. These platforms offer

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access to a wide range of detection technologies, expertise (e.g., in hit-to-lead optimisation, chemoinformatics), and jointly used compound collections.

2.3.1 Compound discovery through compound screening

Screening partner sites provide users access to a large scope of technologies to develop their hit identification projects, such as:

- **Assay development, HTS, and hit profiling services for the identification of active small molecules**. The support includes access to:
  - Assay design and development in a broad range of readouts, including phenotypic assays in BSL2–3 facilities and BSL1 *in vitro* target-based assays.
  - Biochemical and enzymatic target-based HTS, including assay transfer and hit validation.
  - Cell-based HTS, including assay transfer and hit validation.
  - Low- and medium-throughput screening in BSL3 facilities.
  - Fragment screening, including assay development, screening, and hit validation.
  - Hit validation and profiling (e.g., disease-relevant models, ADMET, ROS tox, etc.).
- **Access to small molecules libraries**. Users can access several compound collections at any of our EU-OPENSCREEN screening partner sites:
  - European Chemical Biology Library (ECBL): diversity library composed of 100,000 small molecules, containing approximately 2,464 bioactives.
  - European Fragment Screening Library composed of approximately 1,000 fragments, including 88 minifrags.
  - European Academic Compound Library (EACL): novel compounds submitted by chemists worldwide.
  - Other libraries available at specific partner sites, such as repurposing collections (containing approved and clinical trial compounds), natural compound libraries, etc.

2.3.2 Hit-to-lead optimisation and medicinal chemistry

EU-OPENSCREEN chemistry sites support users with the post-screening hit-to-lead/tool and lead/tool optimisation process. The main services offered are:

- Drug design and evaluation *in silico*.
- Hit-to-lead development following HTS of small molecules.
- Fragment-to-lead development and fragment screening.
- Optimisation of potency, selectivity, and *in vitro*/*in vivo* ADMET properties of small molecule drug candidates.
- Design and synthesis of target degraders (PROTACs, RIBOTACs).

2.3.3 Compound management and quality control

EU-OPENSCREEN operates a state-of-the-art Central Compound Management Facility (CCMF) at its headquarters in Berlin, Germany, which plays an important role in the operation of the RI. EU-OPENSCREEN's integrated CCMF stores the jointly used compound collections and provides the partner sites across Europe with quality-controlled compound sets that may be used to characterise biological activities within user projects. The fully automated CCMF enables cost-effective and reproducible dispensing, copying, and reformatting of microplates in various formats (96/384/1536) depending on the needs of the partner sites and users. It can also accommodate

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these variable needs by accurately selecting individual compounds from the collections for customised sets.

Using liquid chromatography mass spectrometry (LC-MS), the CCMF team quality-controls all EU-OPENSCREEN compounds, including compounds that are submitted by external chemists, to ensure the identity and purity of the compounds which are used by all affiliated partner sites in the scientific user projects. This quality control process is an important component of EU-OPENSCREEN's quality assurance and contributes to the reproducibility of the data generated in scientific user projects.

2.3.4 Open-access Database

The FAIR data guiding principles were developed and are widely applied to improve the Findability, Accessibility, Interoperability, and Reusability of scientific data. EU-OPENSCREEN operates the open-access European Chemical Biology Database (ECBD), which was developed and is curated by the EU-OPENSCREEN partner site IMG Prague. The ECBD serves as an internal data sharing environment as well as a central data hub designed to FAIRify, share, and disseminate EU-OPENSCREEN data to the wide scientific community. The ECBD contains structural and quality-controlled data of EU-OPENSCREEN's compound collections, bioprofiling and cell painting data, and bioactivity data from the scientific screening projects.

The ECBD is a web portal with powerful search and analysis capabilities and contains validated output from screening centres in both a public and a pre-release environment (based on EU-OPENSCREEN's data publication policy with an optional embargo period of up to three years; this period can be extended to a maximum of six years).

Data links with other relevant public databases, such as the ChEMBL database (https://www.ebi.ac.uk/chembl/) and PubChem (https://pubchem.ncbi.nlm.nih.gov/), will be established in order to increase the visibility and reuse of EU-OPENSCREEN data.

2.3.5 Uncovering bioactivities of submitted community compounds

Organic chemists produce a myriad of compounds, often designed for specific activities against a certain target or phenotype. Typically, only very few compounds (e.g., those with a high activity in a specific assay) are deemed promising for use in further studies. Thus, despite the significant effort, time, and resources invested to produce the original set of compounds, the vast majority are ultimately stored unused. Furthermore, compounds with a low activity against the target for which they were synthesised may be active and useful against another target or in an unrelated assay. Natural products also exhibit a rich diversity of valuable scaffolds, but many researchers have only limited access to such natural products. Unfortunately, natural product chemists and organic chemists who synthesise compounds often have limited opportunities to systematically test their compounds against a wide variety of biological targets and uncover these hidden biological activities. The consequence is that too many compounds remain unused and inaccessible for other researchers.

With the aim of making this rich chemical resource accessible to a broader scientific community, and to allow chemists to uncover novel bioactivities of their compounds, the publicly funded open-access initiative EU-OPENSCREEN offers chemists the opportunity to make their compounds available, in a regulated and transparent framework, to a wider community of biologists who can test then these compounds in suitable bioassays. By doing so, chemists can expose their compounds to a broad range of different biological/drug targets to uncover the unknown

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bioactivities of their compounds, which would otherwise not be practical through individual one-to-one collaborations. Once a compound from an EU-OPENSCREEN compound library has been identified as a validated hit compound, a research collaboration between the chemist (who submitted the compound) and the biologist (who developed the bioassay) can be initiated.

2.3.6 Bioprofiling and cell-painting of compounds

All EU-OPENSCREEN compounds are characterised in a suite of cell-based, biochemical, and physicochemical assays to analyse their physicochemical and biological properties: solubility, light quenching/autofluorescence, interference with commonly used bioluminescence reporters, oxidative potential, cellular toxicity, anti-bacterial (Gram-negative and Gram-positive), and antifungal activity. Furthermore, EU-OPENSCREEN uses cell-painting to morphologically examine the effects of compounds on cells. The cell-painting data and morphological profiles are then made available to the scientific community. This will represent one of the largest openly available datasets of its kind, positioning EU-OPENSCREEN as a key player in the field.

Bioprofiling generates a wealth of quantitative data on and rich annotation of each compound. The bioprofiling data enables the early identification of a potential assay readout interference, thereby facilitating the elimination of false positives in screening projects and supporting the selection of high-value compounds for further optimisation. This ensures that results generated in screening campaigns are reliable, reproducible, and comparable, thereby also helping to set superior standards in the field of early drug discovery and preclinical research.

The bioprofiling of submitted compounds increases the value of these compounds and provides the submitting chemists with a range of valuable data on the properties and bioactivities of their compounds. This creates a strong incentive for chemists to share their compounds with EU-OPENSCREEN.

2.3.7 Training

RIs contribute to the excellence in science in Europe and depend on highly qualified personnel for the management and operation of the RIs. Regular training is critical for both RI staff and scientific users to maintain excellence in science.

EU-OPENSCREEN organized training activities over the past years, including webinars, practical workshops, technical training for partner sites, and staff exchanges. Training activities for external users have attracted hundreds of scientists worldwide over the past five years. Unfortunately, in-person training activities were heavily affected by the Covid-19 pandemic. There will be annual training calls for EU-OPENSCREEN partner sites, which are supported by EU-OPENSCREEN central budget. Different formats are supported: (i) practical training workshops organised by partner sites, (ii) external training of technical staff at partner sites, and (iii) staff exchanges between partner sites as well as with external partners to acquire practical hands-on knowledge from expert centres. Furthermore, the EU-OPENSCREEN Central Office organise regular webinars, which focus on different aspects in drug discovery.

EU-OPENSCREEN's annual online training school has been very successful over the past years and attracted many early-career scientists and researchers from overseas. EU-OPENSCREEN will organise the first in-person training school and examine if this format complements the virtual training school. Furthermore, international training workshops will also be organised in collaboration with local partners outside of Europe, to engage with non-European scientists and broaden the geographical impact of EU-OPENSCREEN. In 2024, EU-OPENSCREEN organises with

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the H3D/University of Cape town a sub-Saharan training workshop in drug discovery in Cape Town, South Africa. A second training workshop will be organised in Latin America. In collaboration with EU-OPENSCREEN's Industry Liaison Office (ILO), industry training programs with industry partners will be organised.

The project management of scientific user projects is complex and demanding and requires specialized training. While external project management training courses are available, they do not cover all the required aspects of project management and are not optimal for many partner sites. A working group with managerial staff of EU-OPENSCREEN and the partner sites will be established to map the training needs of managerial staff. Staff exchanges for managerial staff will be organized to establish a process by which partners can efficiently exchange best practices and experiences in managing the local technology platforms, such as service provision, access procedures, and coordination of scientific user projects. Regular workshops will be organized to exchange experiences and different management tools in larger groups. Partners will also have the opportunity to obtain external training in project management.

2.4 New services

2.4.1 Chemoproteomics

Target identification and advanced mass spectrometry imaging (MSI) are important in drug discovery to elucidate the mechanism(s) of action (MoA) of lead compounds. These services have not yet been available within EU-OPENSCREEN. With the integration of a new chemoproteomics partner site category for these technologies and the planned selection of the first such partner sites in 2024, EU-OPENSCREEN will be able to support scientists with chemoproteomics and MSI services starting in late 2024. With such services in place, EU-OPENSCREEN will be able to facilitate the discovery of new therapeutic targets and identification of novel MoA linked to compounds identified in phenotypic drug discovery using disease-relevant *in vitro* models with high intrinsic predictive value for clinical translation. These approaches will also help advance the understanding of the MoA of compounds in the context of their interactions with cells, off-target effects, and underlying liability and toxicity-associated mechanisms. MSI will help quantify the distribution of compounds and their pharmacodynamic (PD) responses at the multicellular and tissue level.

2.4.2 Fragment-Based Drug Discovery (FBDD)

An alternative approach to HTS with comprehensive libraries of small molecules (with a typical molecular weight over 350 Da) is fragment-based drug discovery (FBDD). Fragments are relatively small molecules with a molecular weight below 300 Da. NMR, X-ray crystallography, and other biophysical methods are used for the screening of fragment libraries of around 1,000 fragments. Recently, EU-OPENSCREEN started to use FBDD in scientific user projects, often in cooperation with structural biology partners, and will continue to support scientists in this technology area. The identified fragment 'hits' will be further progressed by EU-OPENSCREEN chemistry partner sites.

2.4.3 Marine Natural Bioprospecting

Due to the high biodiversity of marine ecosystems, marine organisms represent a major reservoir of natural product diversity. Such organisms include marine invertebrates (sponges, cnidarians, bryozoans, molluscs, tunicates, and echinoderms); phytoplankton; green, brown and red algae; marine and intertidal plants; and a broad diversity of microorganisms which often form symbioses

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with other species. Natural products are produced by living organisms to respond the external stimuli, to communicate with the environment, and to serve competition and defence purposes, among other roles in the ecosystem. Interest in the exploitation of the marine environment for novel bioactive natural products has continued to grow exponentially in recent decades, and today, many products and applications have reached the market or are used in human health. In addition to drug discovery, there is also a great interest in marine-derived products as nutraceuticals. Marine derived products often contain active ingredients such as vitamins, enzymes, antioxidants, and essential oils which are used as natural additives in foods and could have beneficial health effects. The cosmetics industry is also looking for novel marine molecules.

Today, the expertise and technical support required to establish a comprehensive discovery pipeline remains scattered throughout Europe. Such resources, facilities, and critical equipment are distributed across multiple institutions, universities, and research groups, hindering access for external scientists. Over the next three years, EU-OPENSCREEN will consolidate its internal capabilities and expertise, which is available at individual local partner sites, and coordinate the development of an integrated RI solution for marine bioprospecting in Europe across three existing RIs: EU-OPENSCREEN, EMBRC, and ELIXIR. The role of EU-OPENSCREEN in this project will be to support external scientists in the area of marine natural bioprospecting as an integral part of its operation. EU-OPENSCREEN partners develop strains and extract libraries, provide chemical and biological profiling of marine extracts, scale-up/proof-of-concept purification of natural products, analytical approaches for the characterization and elucidation of the compound structures, and integration of synthetic approaches and in silico tools to expand the chemical diversity of marine natural products and improve their efficacy.

2.5 Develop future services

The increasing complexity of modern drug discovery projects, however, requires an even more comprehensive portfolio and the integration of other emerging technologies. Over the next five years, EU-OPENSCREEN will expand its catalogue of services and capabilities by integrating emerging technologies in the key areas in drug discovery (e.g., artificial intelligence/machine learning [AI/ML], innovative advanced disease models combined with RNAi- and CRISPR-based genetic approaches, and new chemical targeting modalities such as targeted protein degraders). These advanced services and capabilities will allow EU-OPENSCREEN to better address a wider range of biological targets and develop novel potent and selective biologically-/pharmacologically-active compounds.

2.5.1 New chemical modalities

EU-OPENSCREEN, alongside its medicinal chemistry partner sites, will develop and integrate a concept to support scientists in the development of chemical modalities that can target challenging targets beyond traditional small molecules. These include new chemical probes (e.g., fluorescent, activity-base, and traceless proximity probes), targeted degraders (e.g., heterobifunctional degraders like PROTACs or RIBOTACs), enzymatic modulators, and multitarget molecules associated with polypharmacology. Medicinal chemistry and biological screening sites will work closely together to develop these services based on the expertise and capabilities available at the individual partner sites. The new services will be tested and validated in demonstrator projects before integrating them into EU-OPENSCREEN's offerings for external users. The collaboration between multiple partner sites and synergies with other RIs and research consortia will ensure the excellence of these services.

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As the discovery of small molecules is the core expertise of EU-OPENSCREEN, this RI is in an ideal position to provide the screening technologies and chemistry expertise for the discovery and validation of such novel chemical modalities and to support researchers by providing access to these services and capabilities.

2.5.2 Artificial Intelligence & Machine Learning (AI/ML)

Over the past five years, there has been an astonishing increase in the impact of AI/ML approaches on drug discovery. Over the next five years, EU-OPENSCREEN will employ a range of artificial intelligence (AI) tools to provide a service for the deconvolution of modes of action of chemical compounds with biological interest, a critical step in the drug discovery process. To demonstrate the utility of AI methods, both cell-based (cell-painting chemotype to phenotype analyses) and biochemical/biophysical (ligand:target interactions) datasets will be employed for training and model generation.

The aim is to build evidence on the added value that such a capability will bring to EU-OPENSCREEN and its scientific user community of medicinal and chemical biologists.

2.5.3 Advanced disease models and functional screening

The success of preclinical drug discovery strongly depends on the ability of experimental cell models to recapitulate human pathophysiology. Over the next five years, EU-OPENSCREEN will establish capabilities and workflows for the validation of bioactive compounds (which have been identified through large-scale screening campaigns) by using cellular models that accurately reflect disease phenotypes (e.g., patient-derived, gene-edited, iPSC-derived, and 3D models). The approach will involve analyses of compounds' MoA through complementary genetic screening approaches (RNAi, CRISPR-Cas9). These orthogonal approaches are necessary to ensure the efficacy and appropriate phenotypic response of the compounds and provide an initial perspective on molecular targets and MoA. These workflows will be added onto existing proteomics methods previously developed within the consortium to provide a complete toolbox for MoA determination. Bespoke expertise and capabilities available at individual EU-OS partner sites will be mapped across the EU-OPENSCREEN network, leading to complementary services in the EU-OPENSCREEN RI's catalogue of services, creating a resource for future scientific user projects.

3 Governance and Stakeholder Engagement

Distributed RIs have various stakeholder groups, which have different needs, priorities, and motivations to participate in and support the RI. The incentives and needs of these different stakeholder groups can vary dramatically. The roles and responsibilities of the different boards in the governance structure are clearly defined to consider the different perspectives and interests of these stakeholder groups. The following schematic demonstrates the governance structure of the EU-OPENSCREEN ERIC:

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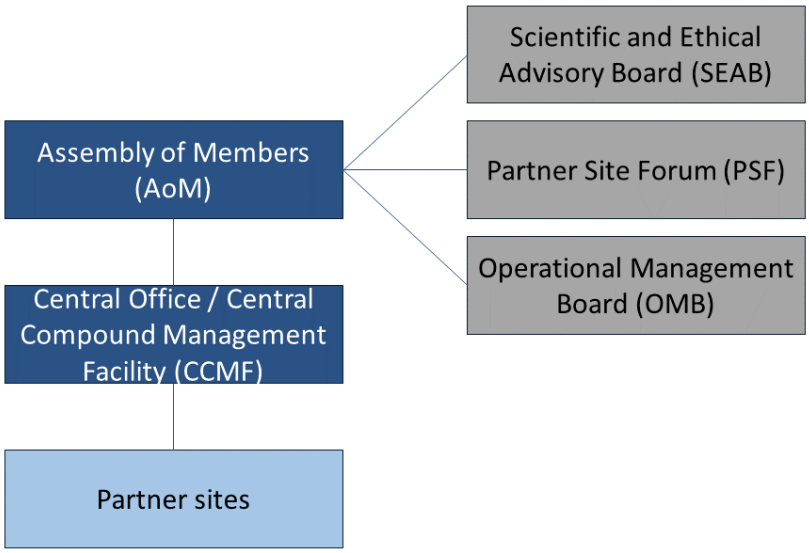

The different boards of the EU-OPENSCREEN ERIC governance and their respective duties and responsibilities are stipulated in the Statutes and Rules of Procedure of the EU-OPENSCREEN ERIC.

3.1 Assembly of Members (AoM)

The Assembly of Members (AoM) is the highest body in the governance the of EU-OPENSCREEN ERIC and holds ultimate decision-making power. The AoM is responsible for the overall direction and supervision of the EU-OPENSCREEN ERIC. The AoM is composed of up to two representatives from each member and observer country. Each member (but not observer) country has one vote and is eligible to host partner sites. The AoM meets twice per year, ideally in person. The AoM discusses, amends, and decides on the strategy, governance structure, intellectual property rights policy, and budget of the EU-OPENSCREEN ERIC. It approves the annual report and work plan and holds the power to appoint, suspend, or dismiss the Director General.

3.2 Director General, Central Office, and Central Compound Management Facility (CCMF)

The Director General is responsible for the efficient administration and coordination of the EU-OPENSCREEN ERIC. The Director General manages the team of the Central Office and the Central Compound Management Facility (CCMF), both of which are located in Berlin, Germany. The Director General and the Central Office team execute the work plan, which is approved by the AoM, including the overall coordination of the research infrastructure, provision of services, access to the research infrastructure, financial accounting and controlling, and legal requirements.

3.3 Partner sites (local nodes)

Partner sites are nominated, evaluated, and formally approved by the AoM. They jointly use the EU-OPENSCREEN compound collections, implement user projects, bio-profile the compounds submitted by chemists, are actively involved in EU-OPENSCREEN training activities, are represented in the Partner Site Forum, and are privileged partners in EU-OPENSCREEN-led Horizon Europe consortia. Partner sites remain organisationally independent of the EU-OPENSCREEN ERIC

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and embedded in their host institutions (e.g., universities, public and private research institutions). Prospective partner sites are evaluated by an independent panel of experts, supported by the EU-OPENSCREEN ERIC Central Office. The expert panel gives recommendations to the AoM, which the approves the positively evaluated partner sites based on the evaluation reports. Following a successful evaluation and confirmation process, the EU-OPENSCREEN ERIC and the new partner sites sign legal collaboration agreements, which are identical for all affiliated partner sites within the same partner site category (i.e., screening, chemistry, and database hosting sites) and is aligned with the Statutes (Article 11) and the Rules of Procedure of the EU-OPENSCREEN ERIC.

3.4 Partner Site Forum (PSF)

All partner sites are represented in the Partner Site Forum (PSF), a permanent body in the governance structure which advises the Director General in the development and execution of the annual work plan, budget, and other matters to enable efficient interaction between the Partner Sites. The PSF plays an important role in advocating for the needs and interests of the Partner Sites within the EU-OPENSCREEN ERIC, emphasising the key role of partner sites in the operation of the EU-OPENSCREEN research infrastructure. The role of the PSF is described in the Statutes (Article 16) and the Rules of Procedure of the EU-OPENSCREEN ERIC.

3.5 Operational Management Board (OMB)

The Operational Management Board (OMB) is composed of three delegates of the AoM (including the Chair and Vice-Chair of the AoM) and the Chair and Vice-Chair of the PSF. The OMB is a permanent body to strengthen the link between the AoM, the PSF, and the Director General. The OMB convenes regularly and supports the Director General to prepare the content for the biannual AoM meetings and serves as a permanent contact point to facilitate the communication between the AoM, PSF, and Director General. The role and tasks of the OMB are described in the Rules of Procedure (Article 3).

3.6 Scientific and Ethical Advisory Board (SEAB)

The Scientific and Ethical Advisory Board (SEAB) consists of independent and internationally recognised scientists and experts who advise the AoM on scientific, technical, and ethical matters. The SEAB provides valuable recommendations to the AoM on EU-OPENSCREEN's scientific performance, technological and scientific developments and their potential integration into the research infrastructure, and ethical issues. The SEAB works closely with the Director General and meets regularly (usually once per year). The duties and responsibilities of the SEAB are stipulated in the Statutes (Article 17) and the Rules of Procedures (Article 3).

4 Outreach activities

EU-OPENSCREEN will leverage communication activities to raise awareness of EU-OPENSCREEN services and capabilities, complement its current training activities, broaden its user base, and ultimately ensure the long-term sustainability of the ERIC. A tailored communication strategy positions the ERIC as the leading RI for chemical biology and early drug discovery in Europe, as

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recognised by researchers, RI user communities, funders, policy makers, and industry communities. The main aims of the strategy are:

- To raise awareness of EU-OPENSCREEN's services, internationally and among European industry;
- To communicate the role, relevance, and accomplishments of EU-OPENSCREEN as a single point of access for expertise, technology, and services in chemical biology and early drug discovery in Europe and beyond;
- To link the results from EU-OPENSCREEN's projects to scientific excellence; and
- To promote and demonstrate impact of EU-OPENSCREEN results on the development of new therapeutics to improve human health.

EU-OPENSCREEN's communication plan is based on the 'RI-VIS Communication Toolkit for European RIs' and includes a detailed analysis of the target audiences, agreed messages, and chosen dissemination channels which will be used over the coming years. In a separate deliverable, D1.4 'Socio-economic impact study and documented refined KPIs', we describe metrics that are collected to monitor outreach activities, which will in turn allow the ERIC to implement solutions to maximise the communication and dissemination of results and achievements, ultimately increasing their impact.

5 Financial sustainability

The majority of the funding for the establishment and operation of RIs is provided by public funders. In the case of European Research Infrastructure Consortia (ERICs), their respective groups of RI member countries provide the core funding of the RI, which is complemented by EU project funding and other revenue sources. These funders regularly evaluate the outcomes of and returns on their investment.

5.1 Financial contributions of members and observers

EU-OPENSCREEN was inaugurated as an ERIC in April 2018 by seven countries: the Czech Republic, Finland, Germany (host country), Latvia, Norway, Poland, Spain. Denmark was an observer in 2018 and became a member country in 2019. In 2022, Portugal and Sweden joined the EU-OPENSCREEN ERIC as the ninth and tenth member countries. Over the past years, there was a focus on increasing the number of member countries by engaging with candidate countries to coordinate and support discussions/negotiations between their local partners and respective research ministries, taking into account their precise needs, funding situations, national roadmap procedures, and governmental requirements. New members increase the geographical footprint of EU-OPENSCREEN and reinforce the engagement with scientists outside the current 10 member countries (via reduced compound replenishment fees, inclusion in EU proposals, improved access to ERIC training activities, etc.). EU-OPENSCREEN will continue to engage with individual candidate countries, applying a country-specific approach with 'roadmaps towards membership' with local 'ambassadors' in candidate countries, such as Greece, Hungary, Israel, Italy, the Netherlands, Romania, and Switzerland.

The founding members were committed to support the EU-OPENSCREEN ERIC for a minimum duration of five years, which ended in March 2023. In principle, founding members are now eligible to withdraw their support. Research funding, including for RIs, is currently under pressure due to factors such as high inflation, the COVID-19 pandemic, and geopolitical tensions. With the aim to

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maintain a stable number of members, which jointly fund the operation of EU-OPENSCREEN, the benefits and rewards of participating in the research infrastructure must be communicated regularly and in a transparent manner to the local partner sites and their funding authorities.

The member and observer countries jointly support the operation of the EU-OPENSCREEN ERIC through their individual membership fees. The annual budget is approved by the AoM, and the contributions of the individual members and observers are calculated based on the funding model as described in the Statutes, Annex 2. In brief, 25% of the budget is distributed equally among the members and observers. The remaining 75% of the budget is then distributed among observers and members using the following financial model:

(GDP per capita – 8,000€) * population size

Observers pay 0.3% of their nominal contribution, and the host country pays a double membership fee. No country shall pay more than 50% of the aggregated contributions of all members.

5.2 Membership benefits for members and observers

Participating in EU-OPENSCREEN has significant benefits for member countries. With the aim to communicate these benefits clearly and transparently to current members, a report of the benefits and activities will be prepared for each country and updated on an annual basis. Furthermore, workshops will be regularly organised to ensure each member country's continued support over the coming years.

The main benefits for participating EU-OPENSCREEN member countries are:

- Only member countries are eligible to host partner sites;
- Privileged access for scientists (e.g., discount of the compound replenishment fee for biologists who have developed an assay and wish to use the EU-OPENSCREEN compound library);
- Only partner sites receive access to (i.e., physical aliquots of) the EU-OPENSCREEN compound collections;
- Privileged partnership in EU-OPENSCREEN-led Horizon Europe projects;
- Improved access to research collaborations with international scientists; and
- Increased collaboration between partner sites.

5.3 Third-party funding

Horizon Europe calls represent an important funding source for EU-OPENSCREEN and its collaborative projects with scientific users and other RIs. EU-OPENSCREEN participates in several projects, detailed below, which receive funding through the European Union's 'Horizon Europe' research and innovation programme:

- The INFRA-DEV projects 'IMPULSE' (March 2024–February 2027) and 'EUREMAP' (January 2024–December 2026) are key EU projects for EU-OPENSCREEN. These projects will help EU-OPENSCREEN to develop its research infrastructure by improving access procedures, expanding the service portfolio, supporting data reproducibility, and exploring new areas where EU-OPENSCREEN can develop novel services.

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- As part of the Horizon Europe projects ISIDORe, canSERV, and AgroServ, open calls for scientific transnational access projects are organised, through which EU-OPENSCREEN implements scientific user projects.
- Horizon Europe projects, such as BY-COVID and EOSC4Cancer, focus on scientific data which are generated in scientific user projects using EU-OPENSCREEN's compound collections.
- The ERIC Forum 2 brings together established ERICs from across scientific fields and facilitates the exchange of experience and engagement with national funding organisations. It also serves as an important platform through which EU-OPENSCREEN can communicate with European science policy stakeholders.

The Central Office will continue to coordinate EU-OPESCREEN-led consortia and ensure the participation of EU-OPENSCREEN and its partner sites in various Horizon Europe consortia. The partner sites are privileged partners.

5.4 Engagement with industry partners, charities and foundations

Until now, most of the funding for the EU-OPENSCREEN ERIC is provided by the member countries and through Horizon Europe project funding. EU-OPENSCREEN will continue to leverage partnerships with other RIs and stakeholders to enhance the cross-RI and cross-country collaborations and to coordinate communication with European and national policy-makers and funding organisations.

New models for pre-competitive models with partners from industry, charities, and foundations for scientific projects will be developed with the aims of diversifying funding and increasing the innovation potential of the RI. A catalogue of services beyond current capacities will be drafted. The newly established Industry Liaison Office (ILO) will play an important role in coordinating discussions with industry partners about their needs and incentives to collaborate with EU-OPENSCREEN. Scientific pilot projects will be implemented with disease-focussed charities and public–private partnerships. Flexible 'case-by-case' models for different private–public partnerships will be pursued.

5.5 Preliminary budget for 2024-2028

The preliminary budget for 2024–2028, with the planned expenses and income from the contributions of individual members, observers, and other funding sources (e.g., third-party funding, compound replenishment fees) for the upcoming 5-year period, has been presented to and discussed by the AoM. The presented preliminary budget is based on a conservative estimate and considers only the income from current members and observers and the income from secured Horizon Europe grants. No other income has been considered from submitted project proposals or contributions from candidate countries that may join as members or observers in the near future. The expenses are based on actual expenses for the current staff at the Central Office and CCMF, the operation and maintenance of the EU-OPENSCREEN database, training and outreach activities, and other expenses. Funding to continue the compound submission model and bioprofiling of submitted compounds is also secured until early 2027. A contingency budget to fund any potential repair or replacement of essential equipment in the Central Office and CCMF

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has also been included. Overall, the financial sustainability of the research infrastructure has been secured at least for another five years.

6 Conclusion

Based on the experience from the first five years of the operation of the EU-OPENSCREEN ERIC and the outcome of the EU-OPENSCREEN-DRIVE project, a comprehensive concept plan and financial sustainability model has been developed for the next five-year period between 2024 and 2028, which is described in this report.

In summary, the ambition is to improve current services and to develop and integrate new services which further expand the service portfolio and capabilities in the areas of AI/ML, new chemical modalities, and complex cell assays.

The expanded service portfolio, which is offered by a consortium of over 30 partner sites across Europe, will ensure that EU-OPENSCREEN continues to offer relevant services and support scientists in the development of chemical probes and drug leads. Through reinforced and targeted outreach activities, EU-OPENSCREEN aims to attract new user groups and increases its scientific and economic impact.

EU-OPENSCREEN aims to secure the support of current members and observers, while simultaneously discussing the benefits of joining EU-OPENSCREEN with candidate countries. Collaborations with industry partners, public– private partnerships, and charities will be reinforced in order to attract funding for the scientific user projects and to diversity the financial support. A preliminary budget for 2024–2028 is available, which ensures the financial sustainability of the EU-OPENSCREEN ERIC for at least the next five years.

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