D3.2: Report on outcomes of the chemical optimisation projects

Version 1.0 – 2023-10-31

for

H2020-INFRADEV-2018-1

(Development and long-term sustainability of new pan-European research infrastructures)

Research and Innovation Action (RIA)

Action Acronym:

EU-OPENSCREEN-DRIVE

Action Full Title:

“Ensuring long-term sustainability of excellence in chemical biology within Europe and beyond”

Grant Agreement No.: 823893

Dissemination level: public

Document Properties:

Deliverable	D3.2: Report on outcomes of the chemical optimisation projects, including of gaps in medicinal chemistry services and recommendation for process improvements for EU-OS operation
Responsible partner	EU-OS
Contributing partners	EU-OS, HZI (screening site), CIPF (screening site), UH-FIMM (screening site), UiB (screening site), MU (chemistry site), DTU (chemistry site), CSIC (chemistry site), OSI (chemistry site), FVB-FMP (chemistry site).
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Due date	31-08-2023
Delivery date	31-10-2023

Table of Contents

This project has received funding from the European Union´s Horizon 2020 research and innovation programme under the grant agreement No. 823893

1 Introduction

EU-OPENSCREEN (EU-OS) is the European Research Infrastructure Consortium (ERIC) for chemical biology and early drug discovery. Established in 2018, EU-OS offers access to state-of-the-art high-capacity screening and medicinal chemistry services throughout Europe for the development of small molecule tools and lead compounds. EU-OS services are currently provided by over 30 partner sites in 10 member countries across Europe (CZ, DK, ES, FI, LV, NO, PL, PT, SE, and DE as host country). It operates an open-access database, the European Chemical Biology Database (ECBD),[1] hosted in Prague at IMG, and a central compound management facility (CCMF) in Berlin, Germany, which stores, quality –controls, and manages the jointly used EU-OPENSCREEN compound collection.[2] The latter is comprised of approximately 100,000 commercially sourced compounds (the European Chemical Biology Library [ECBL]) and a growing number of academically sourced compounds (the European Academic Compound Library [EACL]), all of which are used in high-throughput screening assays at screening partner sites.

In 2019, EU-OPENSCREEN-DRIVE (EU-OS-DRIVE) started as a European Union HORIZON 2020 project to ensure the long-term sustainability of EU-OS operations by promoting measures for i) widening awareness within the academic and industry spheres for its services and data, ii) growing the capacity and competence in the field of chemical biology and early drug discovery across Europe, and iii) developing the management processes needed for a large, distributed infrastructure.

The overall objective of work package (WP) 3 within EU-OS-DRIVE is to provide external scientists with trans-national access (TNA) to screening platforms and medicinal chemistry groups. These groups represent the first generation of users after the inauguration of the ERIC in 2018. In fact, EU-OS-DRIVE aims to increase user trust in existing EU-OS screening and medicinal chemistry capacities—a key prerequisite for running a sustainable research infrastructure (RI). A valuable benefit of TNA is the ability to foster interdisciplinary cross-European collaborations, involving both users and EU-OS partners to ultimately accelerate the early drug discovery process.

Within WP3, the TNA screening projects implemented between 2020 and 2022 (open call in 2019) generated the first comprehensive bioactivity datasets to be uploaded to the ECBD in accordance with the FAIR principles (see Deliverable 3.1, “Report on the outcomes of the screening projects”).[3] In 2022, five successful screening campaigns have advanced to medicinal chemistry programs at five EU-OS chemistry groups to develop the first generation of "chemical tools"/lead compounds; these projects are focus of this report.

[1] https://ecbd.eu/
[2] https://www.eu-openscreen.eu/services/compound-collection.html
[3] https://drive.eu-openscreen.eu/fileadmin/user_upload/221031_DRIVE_Deliverable_D3.1_Report_on_outcomes_of_the_screening_projects_FINAL.pdf

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2 Report on the deliverable

Deliverable 3.2, "Report on outcomes of the chemical optimisation projects, including identification of gaps in medicinal chemistry services and recommendation for process improvements for EU-OS operation", describes the overall outcomes (up to October 2023) of the chemistry projects awarded funding from the medicinal chemistry call in 2021/2022. Primary hits from five successful screening campaigns funded within EU-OS-DRIVE were optimised to derive lead compounds or chemical probes. These successes demonstrate how access to the ERIC can help scientists to develop their chemical biology projects using the complete pipeline of EU-OS services, from hit identification using high-throughput screening (HTS) technologies to hit-to-lead (H2L) and lead optimization phases. Subsequently, we report on the current gaps in medicinal chemistry services and discuss strategies to improve the access processes implemented for the EU-OS operation.

2.1 TNA internal medicinal chemistry call

2.1.1 Overview of the call

Researchers who accessed EU-OPENSCREEN screening facilities via EU-OS-DRIVE for hit identification projects using the ECBL were invited to apply to the internal medicinal chemistry call. Two internal calls for proposals were launched in September 2021 and February 2022.[4] Only successful screening campaigns with identified and validated hit compounds were eligible to apply and establish collaborations with EU-OS chemistry sites. Using the EU-OS-DRIVE funding, up to five H2L projects were funded by the European Commission (EC) (see 2.1.2).

During the preparation of the medicinal chemistry call, access modalities such as application and review processes for chemistry projects were developed to ensure user access to EU-OS facilities.[5]

TNA modalities and review procedures are published online.[6] We adopted a two-step review process composed of a scientific evaluation followed by a technical review. We identified suitable external reviewers, developed the scientific and technical evaluation forms for proposal review, and organized the practical details of evaluation (e.g., communication with the reviewers, introduction to and assistance with ARIA, evaluation follow-up, etc.). Medicinal chemistry partners (MU, FVB-FMP, DTU, CSIC, and OSI) were involved in the design and preparation of TNA modalities and review procedures. Such procedures are now used at the ERIC level for enabling user access to chemistry sites. Work package partners contributed to WP3 activities by supporting the EU-OS management team on the definition of the parameters for the scientific and technical evaluation and by participating in the technical review of proposals and the final selection process.

[4] https://drive.eu-openscreen.eu/drive-startseite/calls/medicinal-chemistry-call-2021.html
[5] https://www.eu-openscreen.eu/fileadmin/user_upload/220617_EU-OS_UserApplicationGuidelines_MEDICINAL_CHEMISTRY_FINAL_v1.0.pdf
[6] https://drive.eu-openscreen.eu/drive-startseite/calls/medicinal-chemistry-call-2022.html

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2.1.2 Awarded chemistry projects

Users from the preceding screening TNA call could test the complete EU-OS service pipeline by allowing them to apply for follow-up optimization of identified compounds. The launch of this TNA call was delayed with respect to the initially planned period (originally month 24 [according to the original workplan], then month 36 [according to Amendment 1, 2021]) as the overall progression of the 13 screening projects during years 2020–2021 was severely affected by the COVID-19 pandemic. Users were eligible to apply if they had generated a set of validated primary hits from the preceding small molecule screening call. Due to delays in the user screening projects, the medicinal chemistry call was split into two subsequent calls (2021 and 2022) to support the screening projects as they were completed. Moreover, to mitigate such delays, also projects with preliminary primary screening data were accepted for submission. Hits coming exclusively from the pilot library were not sufficient for an application.

The chemical optimization support offered under this call covers the following actions:

- Searching for the structure/activity landscape around validated primary hits in databases, as well as for patents to ensure novelty of the observed target-related or disease –model-related activities.
- Assessment of individual validated primary hits regarding their potential for directed chemical modification.
- Recommendation of commercially available analogues for initial structure-activity relationships (SAR) characterization.
- Chemical modifications of validated hits for improvement of specificity, activity, and pharmacological properties.

Moreover, iterative re-screening of chemically modified hits in relevant biological assay was performed in close collaboration with the user and the respective EU-OPENSCREEN screening partner (CIPF, HZI, UH-FIMM) to access compounds' improved properties.

Upon closure of the first call on 15.10.2021, four proposals were submitted by researchers accessing our HTS facilities. The scientific excellence and technical feasibility of the proposals were evaluated following the review procedures set up for this call. Two projects were selected for implementation and two were rejected. The results of the selection process were communicated to the users by 31.12.2021 via an official notification sent through ARIA. By 31.03.2022, the two successful projects, PID18247 and PID18277, were implemented at FVB-FMP (chemistry) and CSIC, respectively.

A second call was launched on 16.02.2022 to accommodate screening projects that were delayed due to the COVID-19 pandemic. Upon closure of the second call on 15.03.2022, an additional four proposals were submitted by researchers accessing our HTS facilities. The four applications were checked for eligibility criteria and submitted to four external reviewers for scientific evaluation and followed by technical evaluation by the relevant partner site. The results of the selection process were communicated to the users on 31.01.2022, and three successful proposals were implemented at DTU, OSI, and MU.

A summary of chemical optimization projects carried out is summarized in Table 1.

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Table 1. Summary of the trans-national chemistry projects awarded for funding during the EU-OS-DRIVE medicinal chemistry call organized in 2021/2022. The status of the projects in September 2023 is indicated.

ID	Research area	Hit series	Screening Partner (country)	MedChem Partner (country)	User country	Project start date	Project status in September 2023
18277	Cancer, neurodegenerative disorders	3	CIPF (ES)	CSIC (ES)	DE	13.01.2022	Completed, publication in preparation
18247	Cancer	2	UiB (NO)	FMP-FVB (DE)	ES	03.02.2022	Hit expansion based on 2 most promising scaffolds ongoing
20647	Cancer, neurodegenerative diseases, infectious diseases, metabolic diseases	1	UiO (NO)	DTU (DK)	FI	05.09.2022	Hit triaging, 12 commercial compounds tested, 6 analogues synthesized, more synthesis needed
20551	Infectious diseases,	1	HZI (DE)	MU (CZ)	ES	08.09.2022	Hits resynthesized and confirmed, analogue synthesis
20659	cancer	8	UH-FIMM (FI)	OSI (LV)	ES	22.11.2022	Hits resynthesis, analogue synthesis

2.2 Outcome of TNA user projects

The general outcome of the five medicinal chemistry projects is described below. Selected projects mainly target cancer, neurodegenerative diseases, and infectious diseases as indication areas. Due to the public nature of this deliverable, sensitive and project-specific information are not disclosed. Successful user stories and publications related to the EU-OS-DRIVE user projects will be disseminated and published on the EU-OPENSCREEN website, as planned in the EU-OS-DRIVE communication and dissemination strategy.

2.2.1 PID18277: Discovery of new modulators of Mitochondria-ER contact sites

Project PID18277 (Table 1), carried out in collaboration with EU-OS screening partner site CIPF and the chemistry site CSIC, both in Spain, allowed researchers from Germany to uncover, optimize, and validate novel MERCS modulators with potential relevance in therapy. [7]

structure–activity analysis and pharmacophore modeliing of hit compounds selected as heads was carried out at CSIC. Three of the most active compounds belonging to three structurally diverse families were selected for optimization. Ninety-five compounds have been synthesized, and its MERCS modulation activity was tested at CIPF in an iterative fashion. Twenty-five compounds have shown interesting MERCS modulating activity. Some even improved the activity values of their parent compounds. Further characterization of their modes of action and pharmacological properties were carried out at the user site. The medicinal chemistry project started in January 2022, and its duration

[7] https://www.eu-openscreen.eu/newsroom/user-stories/ana-garcia-saez-university-of-cologne.html

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was about one year. Results from this collaborative work were presented by the user during the EU-OS-DRIVE final meeting held in Berlin on 20.09.2023, and their publication is in preparation.
In the final feedback survey, the user rated access to the RI as "excellent", thereby validating that open access to RIs greatly improves the research efficiency of European scientists.

2.2.2 PID18247: Targeting SMAD4 protein with small molecules

Researchers from IRB Barcelona are targeting SMAD4, a transcription factor protein mutated in tumors and rare diseases. The long-term aim is to develop specific compounds that interact with their SMAD4 target and i) have pharmacological applications for the treatment of some life-threatening conditions and/or ii) serve as molecular probes for understanding the underlying molecular mechanism.
The project aligns with EU efforts to support research on non-communicable diseases, the leading cause of death worldwide and which are associated with multiple conditions that affect the quality of life of patients.
The project started in 2020 with the validation of SMAD4 as a new viable target during the HTS campaign run at UiB using the ECBL. The successful screening campaign led to the identification of small molecule binders as starting point to develop new therapeutic cures for rare genetic illnesses and cancer.
In 2022, project PID18247 (Table 1) was awarded further EU-OS-DRIVE funding to progress most promising hits in medicinal chemistry project at EU-OS partner site FVB-FMP.
Since February 2022, FMP-FVB has worked on two most promising scaffolds and focused their efforts on hit expansion. Compounds are either purchased from commercial catalogues or synthesized in FVB-FMP laboratories. Optimized compounds are tested at the user site. Results of this collaborative work were presented by the user during the EU-OS-DRIVE final meeting held in Berlin on 20.09.2023.
The user has established a fruitful collaboration with EU-OS partner sites, and the reported work resulted in two PhD theses and a planned publication.

2.2.3 PID20647: Chemical optimization of the tankyrase scaffolding inhibitors

Tankyrases are multifunctional poly(ADP-ribose) polymerases that regulate a variety of cellular processes. In project PID20647 (Table 1), a collaboration between EU-OS screening partner site UiO (Norway) and the chemistry site DTU (Denmark) allowed Finnish scientists to progress in the creation of potent tool compounds to further elucidate tankyrase functions. These tools may validate proposed therapeutic strategies in various disease contexts and may create a potential starting point for further drug discovery/development projects. Since September 2022, staff at DTU have worked on the synthesis of analogues based on hits identified during the HTS campaign performed at UiO. The support at DTU included the analysis of hits (positive and negative), followed by SAR by catalogue. After design of analogues based on one scaffold, six analogues were synthesized. Each compound was prepared following a three- to fourstep synthetic route and was fully characterized. Commercially available analogues of a second hit series were purchased. The other series was prioritized together with the user for compounds synthesis. Screening and evaluation of analogues were performed by the user. These analogues revealed limited information of the SAR after testing. This finding prompted new designs, which have been proposed for further synthesis. To conclude, a blueprint for future

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medicinal chemistry optimization of the hit series has been set by the end of the EU-OS-DRIVE project in October 2023.

2.2.4 PID20551: Chemical optimization of small molecules with antiviral properties

Project PID20551 (Table 1), carried out in collaboration with EU-OS screening partner site HZI (Germany) and the chemistry site MU (Czech Republic), focused on the chemical optimization of small molecules with antiviral properties against the Chikungunya (CHIKV) arbovirus. After a successful screening campaign using the ECBL in a CHIKV screening assay based on a luciferase-expressing recombinant virus performed at HZI, MU started to work on the identified hits in September 2022.
One of the compounds discovered in the screening campaign exhibited notable anti-CHIKV activity and was subjected to detailed characterization. This compound displayed an excellent selectivity index (SI) profile and was proven to inhibit the translation of the CHIKV RNA genome, a critical stage in the virus' life cycle. MU focused on the resynthesis of the hit from the HTS campaign and exploration of early SAR around the hit. In the past year, fourteen analogues were synthesized to pinpoint the active site. In fact, iterative re-screening of compounds in relevant biological assays was further supported by the screening group at HZI. Two of the newly prepared analogs were comparably/ more active than the original hit. Follow-up steps will involve conducting *in vivo* assays using mouse models at the user site.
Results from this collaborative work were presented by the user during the EU-OS-DRIVE final meeting held in Berlin on 20.09.2023. At least one publication is planned.
Through EU-OS-DRIVE TNA screening and medchem calls, the user was able to access the RI with expertise that was unavailable at the user's laboratory and rapidly progress their discovery project.

2.2.5 PID20659: Development of retinoblastoma modulators

Project PID20659 (Table 1), carried out in collaboration with EU-OS screening partner site UH-FIMM (Finland) and the chemistry site OSI (Latvia), focuses on the chemical optimization of phosphomimetic retinoblastoma (RB) modulators as a potential cancer treatment. RB protein is essential for the proper modulation of the G1/S cell cycle transition, and its inactivation contributes to deregulated cell proliferation and leads to oncogenesis. The cell-based HTS campaign carried out at UH-FIMM using the ECBL resulted in 116 hits with EC_{50} < 1uM. Filtering off the compounds with a bioluminescence interference gave 14 hits with $EC_{50} \leq$ 1uM. The latter hits were clustered into eight series. One representative from each series was selected based on the following criteria: (a) $EC_{50} \leq$ 1uM; (b) displaying full DR curve. Eight hits were selected for the synthetic H2L phase. In fact, synthesis routes were developed, and re-synthesis was executed for all eight compounds. Based on the synthetic routes, 24 analogues were also generated based on six hit structures. Assessment of the biological activity of these compounds is ongoing at the user site.

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2.3 Identification of gaps in medicinal chemistry services and recommendation for process improvements for EU-OS operation

The EU-OS-DRIVE medicinal chemistry call gave us the opportunity to test scientific platforms at our partner site institutions and the established access procedures within the whole network to evaluate and execute the first set of medicinal chemistry projects. After the conclusion of user projects, a feedback survey is circulated to users and partner sites to evaluate the collaboration and give recommendations for future improvements. The survey addresses the following criteria: i) quality of working in collaboration with EU-OS central office and partner sites; ii) implementation and manageability of the EU-OS-DRIVE medicinal chemistry call and application procedure *via* ARIA; iii) satisfaction with the results and impact on their research.

EU-OS chemistry groups have adequate facilities, analytical equipment and expertise to efficiently optimise screening hits to generate more potent and selective probes, to progress hits into H2L and lead optimisation programs, to design and optimise compounds based on structural information and to initially profile leads/probes in *in-vitro* ADMET assays (e.g. solubility, LogP, PAMPA, microsomal stability, and toxicity).

From the implementation of user projects described under 2.2 we learned that several aspects are critical for an appropriate medicinal chemistry support which aims at delivering thorough results to users in an efficient and timely manner:

- **Access to biochemical and cell-based assays for screening of analogues:** Originally, we anticipated that users would assess the biological activity of compounds provided by their chemistry partner site. However, we experienced that 3 out of 5 user projects relied on EU-OS screening sites for the biological validation of synthesized compounds emphasizing the importance of availability and accessibility of profiling/screening services within the consortium for a smooth progression of user projects. While standard development assays are available at chemistry partner sites, research specific biological assays are usually lacking.
- **Access to biophysical methods and structural characterization techniques:** Often, it is required to validate hit compounds using multiple assays and biophysical techniques to assess compound binding and drive the lead optimization phase. Those methods are not always available at EU-OS chemistry sites. Therefore, the collaboration with the user and/or other research infrastructures specialized in complementary structural biology services are of utmost importance. In 2022, EU-OPENSCREEN signed a Memorandum of Understanding[8] between EU-OPENSCREEN ERIC, Euro-BioImaging ERIC,[9] and Instruct ERIC[10] forming a Consortium on Molecular Life Science Infrastructure Services. The strong and reliable partnership between the different RIs ensures a rapid access to additional technologies and expertise not available within the EU-OS network. Moreover, the three RIs collaborate in

[8] https://www.eu-openscreen.eu/fileadmin/user_upload/221020_MoU__221007_Brno20221020.pdf
[9] https://www.eurobioimaging.eu/
[10] https://instruct-eric.org/

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several EU-funded projects with focus on TNA access such as ISIDORe,[11] CanSERV[12] where users can apply for funding to access multiple services.

- **Access to complex disease models for further validation of lead compounds:** Potent and selective hit compounds require validation in advanced models/ functional assays to assess their performance under physiologically more relevant conditions. To access those capacities, users rely on already existing collaborations or seek for expert sites. In 2024, EU-OS will kick off the EU-funded HORIZON-INFRA-2023-DEV-01 project "IMPULSE", in which partners from KI and UC will lead a work-package to establish capabilities and workflows for the validation of bioactive compounds (identified through large-scale screening campaigns) by using cellular models that accurately reflect disease phenotypes (e.g., patient-derived, gene-edited, iPSC-derived, 3D models). These models will help to create molecules which reliable activity in physiologically relevant conditions. The long-term goal is to include these validation models in the current EU-OS service portfolio and make them easily accessible to the user community.
- **Timelines and resources:** In EU-OS-DRIVE, the resources planned to carry out medicinal chemistry projects span from six to eleven person moths (PM) of staff/researchers working on the project with associated costs for consumables/ reagents. We learned that those resources are very limited for performing a complete H2L or lead optimization project which, depending on the chemistry and complexity, can exponentially exceed the resources available within EU-OS-DRIVE. From above reported user projects outcomes, resources allocated in EU-OS-DRIVE were sufficient to allow partners to work on few hit series and explore the synthesis of a rather lower number of analogues. Cost for retesting of analogues at screening and/or user sites are not included in the initial planned budget. A financing for at least three years would therefore be needed for medicinal chemistry support in early drug discovery projects. Therefore, focus for developing strategy for realizing funds (incl. for cross-RI work,) is needed for a long-term support of the ERIC.
- **Machine learning and artificial intelligence:** Offering the computational screening of the ECBL was never pursued due to the relatively small set of 100,000 compounds. However, there is great value in the data sets produced by the screening sites by using them as foundation for machine learning. Using this source as a starting point allows us to screen through millions of commercially available and billions of theoretical compounds. Potentially, this approach can become a valuable tool to support chemist in finding suitable molecules or prioritizing their acquisition or synthesis. Currently, the consortium is exploring possibilities towards providing this service.
- **Communication:** Maintaining a close communication with service providers and users has been shown as a crucial factor for the success of user projects. Especially in case of delays or difficulties in the technical implementation of the research projects which could lead to additional costs through extra consumables and working hours. It is difficult to find a good solution for these types of issues and to decide upfront when a project is at risk to run out of funds or has to be judged as unfeasible. Therefore, EU-OS tries to always stay in close contact with the user to inform the user about the development and decide together with user on specific case scenario.

  To guarantee efficiency and monitor projects implementation, EU-OS project management team onboards new users through official kick-off meetings, and subsequently collects

[11] https://isidore-project.eu/
[12] https://www.canserv.eu/

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systematic project updates and interim user surveys for each project during the project lifetime. Kick-off meetings bring together the user, EU-OS central office and the partner site and clarify objectives, the plan and timelines of a project. The systematic project updates are requested directly to the partner sites and serve to identify risks that have not been previously reported on an ad-hoc basis. The central office can follow up on incurring issues and mitigate them together with the user and the partner site.

3 Conclusion

Thanks to EU-OS-DRIVE, today EU-OS has processes and frameworks in place to ensure continuous access of European and international researchers to its partner facilities to develop their hit identification and/or H2L and lead optimisation projects. By adopting an open access policy, EU-OS ensures that all screening data generated from user projects is available to everyone, including researchers from academia and industry via the ECBD.

EU-OS-DRIVE supported the ERIC operations with the first call for proposals to access its medicinal chemistry services. Five chemical optimisation projects were successfully implemented. Our access procedures served most of the requirement to give users transnational access to EU-OS. The central office of the EU-OS ERIC acted as a single point of contact for users, organised the call, assisted the users in identifying the appropriate partner site if necessary, monitored the project progress during its implementation phase and continuously collects users and facilities feedback to improve the ERIC operations.

During the last two-years, those access procedures to EU-OS infrastructure developed and piloted within EU-OS-DRIVE were implemented and improved at the ERIC level for users accessing a large catalogue of services offered by >30 partner sites.[13][14] Early success stories of our consortium are published at https://www.eu-openscreen.eu/newsroom/user-stories.html. The strong track-record of our partner sites working on many projects and disease areas[15] are ensuring the quality and efficiency of the services provided by the ERIC. To date and after the first screening and medicinal chemistry calls, the ERIC attracted over eighty user projects requesting access to the HTS facilities and medicinal chemistry support. It becomes apparent that a collaborative approach is key to facilitate the translation of screening results into high quality tool/lead compounds and therefore accelerate small molecule drug discovery. A real impact of this joint effort will be visible in several year until a decade from now as timelines from discovering novel activities to profiled chemical probes or lead compounds in pre-clinical/clinical phases are considerably long. EU-OS ERIC envisions to strengthen its offer for a quicker response to the current needs in the early drug discovery by expanding i) its compound collections with other compound libraries; ii) its services by integrating chemical proteomics capabilities to support the identification of drug-target interactions (e.g. deliverable 1.2 “Handbook and defined user workflows for new categories of partner sites”) and CRISPR/siRNA methods, virtual and fragment-based screening to complement the HTS hit identification with other hit/lead generation methods, and iii) hit validation modalities using more physiologically relevant cellular

[13] https://www.eu-openscreen.eu/services/medicinal-chemistry.html
[14] https://www.eu-openscreen.eu/services/screening.html
[15] Brennecke P, *et al*., SLAS DISCOVERY, **2019**;*24,* 398-413. doi:10.1177/2472555218816276

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models such as patient-derived cells and 3D models for a swift translation of preclinical results into clinical use.

In the long prospective, the further evolution of the ERIC will strive to support a wider user community combining state-of-the-art technologies with multidisciplinary expertise addressing future scientific challenges and/or demands and global emergencies and fostering innovation in Europe and beyond.

To conclude, considering the five EU-OS-DRIVE medicinal chemistry projects the major bottleneck identified in the access was related to difficulties to implement user projects in a time-limited fashion considering the necessity of having iterative cycles of compound testing at user/screening partner site facilities which is time-dependent. Due to the delayed completion of screening campaigns affected by COVID-19 in 2020, 2021, medicinal chemistry projects were postponed starting in 2022. This delay significantly limited the time for implementation of chemistry project to approx. one year.
It is worth to mention, that EU-OS chemistry sites are academic groups and as most of academic laboratories practical limitations based on fundings, and resources can be considered as major drawback if compared with industry/ CRO settings. Proper funding and adequate time for medicinal chemistry projects need to be addressed in the future.

4 Delivery and schedule

This deliverable was postponed to the end of the EU-OS-DRIVE projects allowing the overall progression/completion of the medicinal chemistry projects which were limited in timescale due to a major delay that affected the screening campaigns during the COVID-19 pandemic.

5 Glossary

ADP: Adenosine Diphosphate
ARIA: Access to Research Infrastructure Administration
ADMET: Absorption, Distribution, Metabolism, Excretion and Toxicity
CCMF: Central Compound Management Facility
CHIKV: Chikungunya virus
CIPF: Centro de Investigacion Principe Felipe
CSIC: CONSEJO SUPERIOR DE INVESTIGACIONES CIENTIFICAS
CRO: Contract research organisation
DR: Dose–response
DTU: Technical University of Denmark
EACL: European Academic Compounds Library
EC: European Commission
ECBL: European Chemical Biology Library
ECBD: European Chemical Biology Database
ERIC: European Research Infrastructure Consortium
EU-OS: EU-OPENSCREEN ERIC
EU-OS-DRIVE: EU-OPENSCREEN-DRIVE
FVB-FMP: Forschungsverbund Berlin, Leibniz-Forschungsinstitut für Molekulare Pharmakologie
HTS: High-throughput Screening
HZI: Helmholtz-Zentrum für Infektionsforschung

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H2L: Hit-to-lead
IMG: Institute of Molecular Genetics of the Czech Academy of Sciences
IRB: Institute for research in biomedicine
KI: Karolinska Institute
MERCS: Mitochondria-ER contact sites
MU: Masaryk University
OSI: Latvian institute for organic synthesis
PAMPA: Parallel artificial membrane permeation assay
RI: Research infrastructure
SAR: Structure-activity relationship
SI: Selectivity index
TNA: Transnational access
UC: University of Coimbra
UH-FIMM: University of Helsinki (Finland – Institute for Molecular Medicine)
UiB: University of Bergen
UiO: University of Oslo
WP: Work package

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