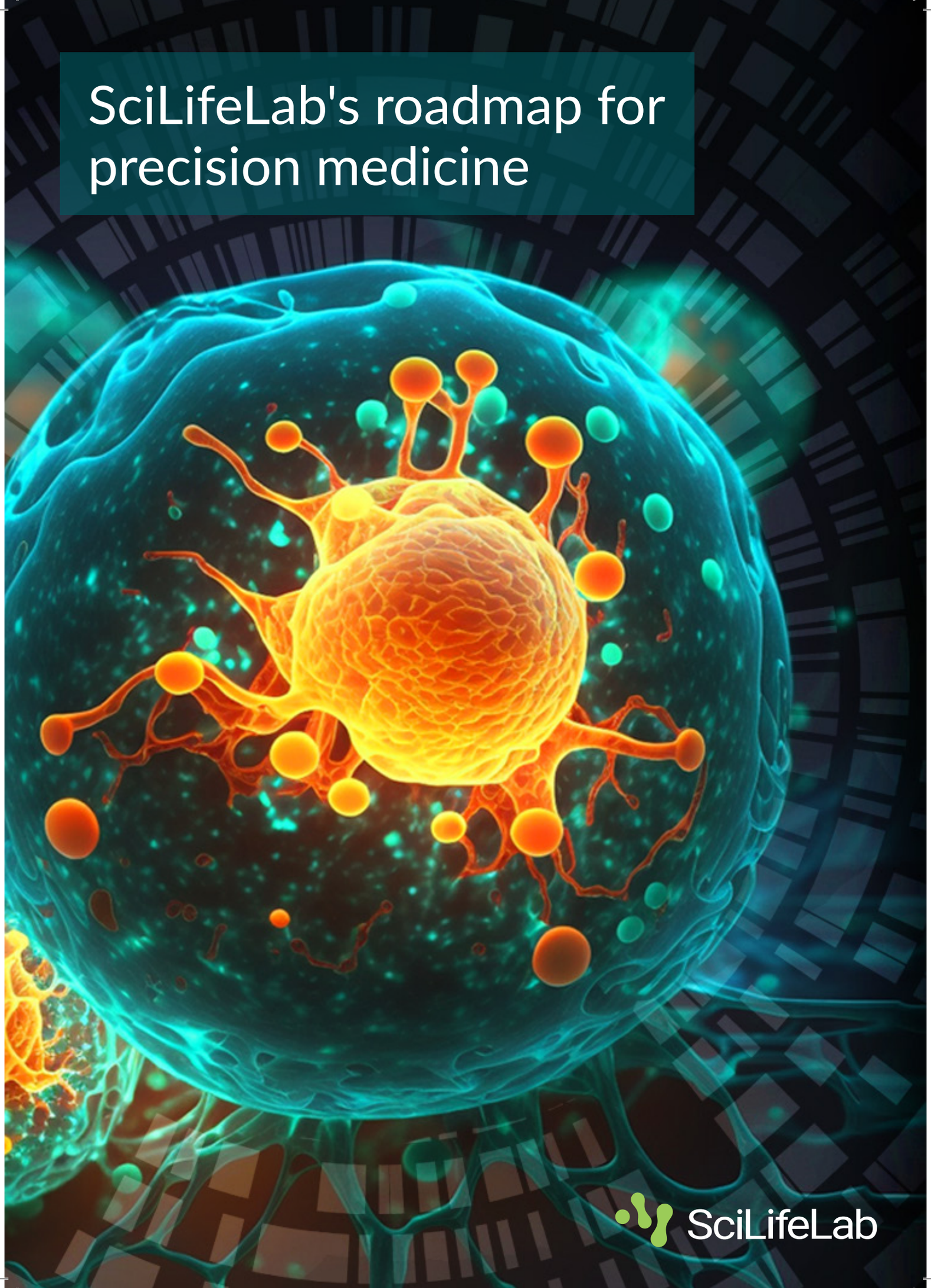
SciLifeLab's roadmap for precision medicine



SciLifeLab

Executive summary

Science for Life Laboratory (SciLifeLab) is a national infrastructure for molecular life science research resting on three pillars: i) a state-of-the-art technology infrastructure, ii) a research community with expertise in technology and computational research, and iii) the Data-Driven Life Science (DDLS) program. Precision medicine is transforming healthcare, and through the Clinical Genomics platform, SciLifeLab has already played a major role in the implementation of genomics-based precision medicine in healthcare.

With its cutting-edge technology and data capabilities, SciLifeLab has potential to be a key player to further accelerate research and implementation of precision medicine. The purpose of the SciLifeLab Precision Medicine capability is to strengthen and coordinate SciLifeLab's efforts within the precision medicine field, both internally and in collaboration with external stakeholders. This Roadmap describes SciLifeLab's contributions towards the vision of Sweden being a world-leading nation in precision medicine through four strategic objectives:

1. Promote technology- and data-driven precision medicine research at SciLifeLab. Establish a precision medicine research community including researchers, infrastructure, healthcare professionals and industry, support collaborative projects driven by clinical need and patient perspective, and promote FAIR (findability, accessibility, interoperability and reusability) data principles.

2. Increase accessibility of the SciLifeLab infrastructure for translational research and clinical studies. Establish workflows for supporting cross-platform research projects, clinical studies and trials, as well as combined analysis of molecular and/or imaging data with clinical data.

3. Enhance awareness and competence on technology- and data-driven precision medicine. Organize training events for the precision medicine research community, and promote outreach activities on a national and international level.

4. Establish effective partnerships between SciLifeLab and key stakeholders in precision medicine. Align SciLifeLab's efforts within precision medicine with other stakeholders such as health care and industry, apply for funding, and ensure that SciLifeLab is in line with international cutting-edge efforts.

Vision and mission

Vision

Sweden is a world-leading nation in precision medicine

Mission

To be a key player in acceleration of research and implementation of precision medicine through technology- and data-driven approaches

Precision Medicine

Precision medicine will significantly improve human health, but the implementation requires continuous collaboration between researchers, technology- and data science experts, healthcare organizations and professionals, industry, patients and society at large. The three pillars (infrastructure, research expertise and DDLS) position SciLifeLab as one of the key players for Sweden to become a world-leading nation in precision medicine. In this Roadmap, we define precision medicine, in agreement with the EU health ministers' definition, as the "*characterization of individuals' phenotypes and genotypes aiming at tailoring the right therapeutic strategy for each patient, to determine the predisposition to disease or to deliver timely and targeted prevention*" [1].

Background

SciLifeLab was initiated in 2010 and encompasses today seven locations across Sweden (Gothenburg, Linköping, Lund, Stockholm, Umeå, Uppsala and Örebro). The SciLifeLab **research infrastructure** aims to provide cutting-edge technologies to enable excellent research in life science, and is organised into ten technology platforms, consisting of > 40 units distributed across the country (Figure 1). SciLifeLab has been engaged in precision medicine since its launch, and an important milestone was the establishment of the Clinical Genomics platform in 2014. Apart from providing end-to-end services for translational and clinical research, the Clinical Genomics platform also adapts and develops new methods for healthcare [2].

The platform has played a key role in the development and implementation of genomics-based precision medicine in Sweden as well as in the launch and continued technology support of Genomic Medicine Sweden (GMS). GMS is a national collaboration project between seven universities and corresponding healthcare regions focusing on the implementation of genomic-based precision medicine [2, 3]. There are great opportunities for increased use of many of the technologies and services offered by the SciLifeLab platforms in precision medicine. Most platforms and units are actively taking steps towards establishing precision medicine research services, in collaboration with the research community (Appendix 1).

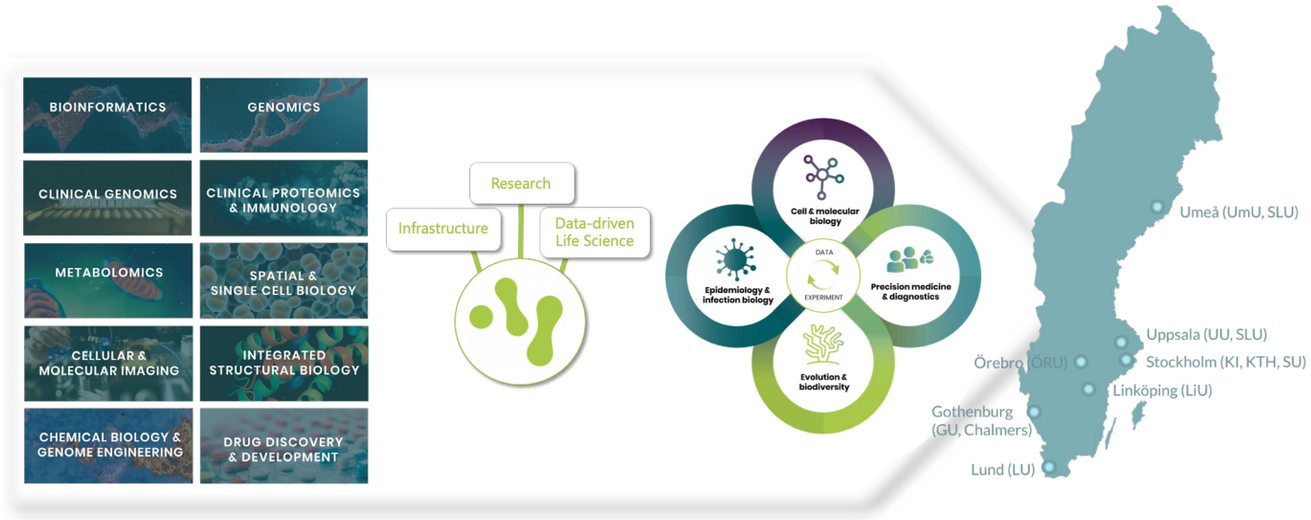


Figure 1. SciLifeLab's three pillars comprise the infrastructure with ten technology platforms, the research community, and the DDLS program with four research areas (Precision medicine & diagnostics, Evolution & biodiversity, Epidemiology & biology of infection, and Cell & molecular biology)". The Precision Medicine capability integrates the three pillars to make SciLifeLab a key player for the acceleration of precision medicine research and implementation on a national level.

The SciLifeLab **research community** consists of over 300 research groups and 1500 scientists across the life science areas. There is a strong focus on molecular medicine research, bioinformatics, and biomarker discovery, and hence an excellent opportunity to promote technology- and data-driven precision medicine [4]. The SciLifeLab research community includes SciLifeLab Fellows and other group leaders across all seven geographic locations, as well as Research Community Programs, the COVID-19 Research Program and the Pandemic Laboratory Preparedness Program. The DDLS program will enrich the national precision medicine research community, along with the Wallenberg Centres for Molecular Medicine (WCMM).

The SciLifeLab and Wallenberg National Program for **Data-Driven Life Science (DDLS)** was initiated in 2021 and is a recruitment, competence building and innovation program funded with a total of SEK 3.1 billion from the Knut and Alice Wallenberg Foundation. DDLS is coordinated by SciLifeLab and has four research areas, one of which is precision medicine and diagnostics. DDLS aims to bridge the gap between data science and life science as well as attract and train scientific expertise. As part of the program, over 150 PIs, postdocs and PhD students in the area of precision medicine and diagnostics will be recruited [4]. The DDLS program also promotes data infrastructure in life science through funding a national *Data Science Node* for each of the four research areas. Karolinska Institutet serves as host for the Data Science Node for precision medicine and diagnostics, which will be an important part of the SciLifeLab Precision Medicine capability.

Taken together, the technology- and data expertise at SciLifeLab offers great opportunities for playing an important role for precision medicine at the national level. However, the expertise, resources and funding are currently scattered throughout different research groups, platforms and sites, and synchronization will increase the potential of SciLifeLab to contribute towards accelerating precision medicine.

Strategic objectives

To outline SciLifeLab's role towards accelerated precision medicine in Sweden, four strategic objectives have been defined (Figure 2).

Figure 2. The strategic objectives towards developing the Precision Medicine capability at SciLifeLab and contribute to acceleration of precision medicine in Sweden.

Each objective is associated with a number of action points. Many of the actions will be coordinated by the SciLifeLab Scientific leads and Scientific coordinator for precision medicine, as well as the DDLS precision medicine and diagnostics area lead and coordinator. However, important contributions will be needed also from other internal and external partners. Internal entities that will be leading these activities within SciLifeLab have been indicated within square brackets after each action. External stakeholders, including GMS, healthcare, industry and biobanks, have not been listed but will play an important role in many of the actions. Moving forward, we foresee a need to form a Precision Medicine Office (PMO) with the operative responsibility for leading the realization of the actions described in this roadmap and a Precision Medicine strategic Expert group (PME) with representatives from the SciLifeLab infrastructure, DDLS, biobanks, and the clinical research community, to ensure broad cutting-edge expertise for decisions and coordination of precision medicine actions across organizations. Input from stakeholders including industry, patient organizations and representatives from Swedish universities at a national level, will be collected through targeted meetings and events.

1. Promote technology and data-driven precision medicine research at SciLifeLab

a. Establish a precision medicine research community with national networking events, workshops, conferences and symposia. The community will build on already existing networks and include researchers, healthcare professionals, the DDLS program, the SciLifeLab infrastructure and industry. [PMO, PME]

b. Launch collaborative research projects driven by clinical need and patient perspective, including clinical technology development projects and evaluation of clinical utility of innovative new methods, to adapt SciLifeLab technologies and services for clinical research questions.
[PMO, SciLifeLab infrastructure]

c. Support users of the SciLifeLab infrastructure in generating FAIR research data sets for data-driven precision medicine research and diagnostics.
[PMO, SciLifeLab Data Centre, DDLS, SciLifeLab infrastructure]

d. Promote the establishment of a national infrastructure/program for biomarker discovery and development.
[PME, SciLifeLab management group]

2. Increase accessibility of the SciLifeLab infrastructure for translational research and clinical studies

a. Establish workflows to support research projects that require rapid processing of clinical samples, including best practices for quality control, analysis of samples one at a time, access to multiple platforms and secure data handling.
[PMO, SciLifeLab infrastructure]

b. Build up competence and support structures for advanced analysis of molecular and/or imaging data combined with clinical data, develop clinical data reporting and support sustainability and dissemination of developed data tools.
[PMO, DDLS, SciLifeLab Data Centre, SciLifeLab infrastructure]

c. Offer SciLifeLab's services for clinical studies and trials and promote integration of research in hospital clinics.
[PMO, SciLifeLab infrastructure, PME, SciLifeLab Data Centre]

d. Take an active role in national and international grant applications to attract funding for realizing the objectives in this roadmap.
[PMO, PME, SciLifeLab infrastructure, research community]

3. Enhance awareness and competence on technology- and data-driven precision medicine

a. Organize national training events related to technology and data-driven approaches for precision medicine, targeted at the precision medicine research community and master students.
[PMO, SciLifeLab Training Hub, DDLS, PME, SciLifeLab infrastructure]

b. Promote outreach activities targeted at the precision medicine research community, healthcare professionals, decision makers, industry, patient organisations as well as the general public.
[PMO, SciLifeLab Training Hub, DDLS, SciLifeLab infrastructure]

c. Support the SciLifeLab community in the process of standardization and accreditation of assays required for clinical applications.
[PMO, PME, SciLifeLab Training Hub, SciLifeLab infrastructure]

d. Establish channels for communication of, e.g., services, training and funding opportunities relevant for precision medicine.
[PMO, SciLifeLab infrastructure]

4. Establish effective partnerships between SciLifeLab and key stakeholders in precision medicine

a. Establish an appropriate organization for precision medicine within SciLifeLab.

b. Align SciLifeLab's precision medicine efforts with those of other key players, including healthcare regions, GMS, ATMP (advanced therapy medicinal product) community, biobanks, precision medicine centres, industry and patient organisations.
[PMO, PME, SciLifeLab infrastructure, SciLifeLab management group]

c. Promote innovation and industry collaboration within technology- and data-driven aspects of precision medicine.
[PMO, PME, SciLifeLab infrastructure]

d. Engage in national and international research and infrastructure projects relevant for precision medicine, including EU funded projects and alliances.
[PMO, PME, SciLifeLab infrastructure, research community]

e. Ensure that SciLifeLab is in line with international cutting-edge and best practices within precision medicine.
[PMO, PME, SciLifeLab infrastructure]

f. Take an active role in discussions related to precision medicine strategies including ethical, legal and social implications in Sweden and internationally.
[PMO, PME, SciLifeLab management group]

Challenges and future directions

Connect technologies with clinical needs

The progression of precision medicine provides improved healthcare for individual patients, as well as an opportunity for equitable healthcare across different patient groups and communities by objective biomarker measurements and data-driven clinical decision support. SciLifeLab will have a significant impact on future precision medicine by being a key player in the development of diagnostic tests, treatments and preventive methods. An important challenge here will be to find the best way to connect the technology experts at SciLifeLab with healthcare professionals, clinical researchers and patient representatives that see the clinical needs. SciLifeLab also has great opportunities to support clinical studies and trials with both technology and expertise. Clinical trials constitute the backbone of evidence-based medicine and are important for testing new treatments as well as for evaluating biomarker performance in clinical settings. New types of innovative trials where baseline profiling with molecular biomarkers and imaging are used to match patients to multiple new treatment options in one trial have recently been introduced, and are expected to further increase the demand of high-quality biomarkers, assays and data analysis capabilities.

Establish clinical grade sample and analysis workflows

Many of the technologies established at the SciLifeLab infrastructure have a strong untapped potential for precision medicine applications, including preventive methods. However, most projects are currently based on already collected samples, where analyses are carried out in batches. In healthcare, but also in clinical studies where results are used for clinical decision support, samples need to be handled in real-time and analysed with a short turn-around time. Furthermore, it is necessary to be able to ensure assay and result quality also for samples with limited material and suboptimal quality. A transition in sample handling is therefore needed to increase the usefulness of the SciLifeLab infrastructure for clinical studies and trials.

Strengthen biomarker discovery and development

Precision medicine and health often rely on biomarkers matching each individual with a particular treatment or preventive strategy. SciLifeLab has a strong profile in biomarker discovery, but taking novel biomarkers from discovery into clinical routine is challenging and support structures for academic biomarker implementation is lacking. A national program for biomarker discovery and development could support in silico and experimental validation of promising biomarkers, including assay development and testing for a point-of-care setting. In addition, support in alignment with the regulatory and legal landscape such as the new European In Vitro Diagnostic Regulation (IVDR), is needed. From 2028, the use of in-house developed tests in healthcare will only be possible if there are no equivalent CE-marked products on the market. The process of CE marking according to IVDR is extensive and costly, which can be prohibitive for researchers and small and medium sized enterprises (SMEs) as well as for investments in products with a limited market. To ensure Swedish academic and start up diagnostics development for precision medicine and health, a national platform is needed bridging academic precision medicine biomarker discoveries to commercialization, similar to SciLifeLab's Drug Discovery and Development (DDD) platform already catalysing academic drug development. Such a bridging function between academic precision medicine biomarker discoveries, biotech SMEs and hospital clinics would likely provide increased opportunities towards implementation of biomarkers also for underserved diseases and communities by connecting academic expertise and lowering the development cost to enter the market and the clinic.

Facilitate data sharing and secondary use of healthcare data

The DDLS program holds promise to enable novel AI-based approaches for analyses of biological and health data. For DDLS to reach its full potential, it will be necessary to increase awareness among researchers about powerful existing data sets and sample collections. However, there are also legal issues related to data sharing and secondary use of healthcare data, which limits many data-driven analyses to exploratory data sets rather than healthcare data. Large data sets often have several owners to involve in the process of granting access to data, and in addition, new research questions may require new patient consent.

Attract funding for clinical research and large-scale projects

Another challenge for realizing precision medicine is funding, and external grants will be important to move the field forward. While SciLifeLab can provide access to infrastructure and expertise in technologies and data analyses, funding for large-scale projects covering all steps from bench to bedside as well as dissemination of best practices learned from these projects will be needed. SciLifeLab is already a partner in a number of national and European projects related to precision medicine, and it will be important to engage the precision medicine research community to fuel new ideas for collaborative projects and attract new large-scale funding. Acceleration of precision medicine is also challenged by the current funding system, where high impact discovery research is often evaluated higher than fine-tuning and validation of technologies and diagnostic tools for routine healthcare. Evaluating the societal impact of grant applications and achievements will be important to enable more patients to benefit from precision medicine.

Establish partnerships with key stakeholders within precision medicine

Precision medicine will need novel organisational designs and thinking to match the incentives and funding schemes of universities, regional healthcare and national infrastructure as well as the private sector. It will therefore be essential to build strong partnerships between SciLifeLab and external stakeholders such as healthcare, industry and patient organizations. No single stakeholder is able to resolve all challenges alone, and it will be important to define the role and contribution of each partner in the joint journey towards better health.

With these challenges in mind, there is still great opportunity in the joint offering of the SciLifeLab infrastructure, research community and DDLS program towards accelerated precision medicine. By enabling novel sample flows, systematic biomarker research and diagnostic assay development we will continue to support not only cutting-edge precision medicine research but also clinical studies and trials towards increased health and societal benefit.

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List of abbreviations

ATMP	Advanced Therapy Medicinal Product
DDD	Drug Discovery and Development
DDLS	Data-Driven Life Science
FAIR	Findability, Accessibility, Interoperability and Reusability
GMS	Genomic Medicine Sweden
IVDR	In Vitro Diagnostic Regulation
PME	Precision Medicine strategic Expert group
PMO	Precision Medicine Office
SciLifeLab	Science for Life Laboratory
SME	Small and Medium sized Enterprise

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Appendix 1

Examples of services established at the ten SciLifeLab platforms that are relevant for precision medicine, as well as ongoing efforts to establish such services. More information about services provided by each platform is available at the website: https://www.scilifelab.se/services/

The **Bioinformatics platform NBIS** provides the precision medicine community with advanced hands-on bioinformatics project support, infrastructure and training. NBIS has extensive experience of sensitive data and participates in prominent EU projects, e.g., GDI (Genomic Data Infrastructure) enabling the European 1+ Million Genome Project, BigPicture for digital pathology, and EUCAIM for cancer image data. NBIS hosts EGA-SE – the Swedish node in the federated European Genome-phenome Archive. Furthermore, NBIS data management support promotes FAIR data sharing and assists users with data publishing in precision medicine research. NBIS enables advanced medical image analysis through our AIDA data hub and bioimage informatics units.

The **Genomics Platform** and National Genomics Infrastructure provide many services relevant for precision medicine: whole-genome and targeted sequencing (short & long-read, 16/18S), RNA-seq (short & long-read), SNP genotyping, plasma proteomics, DNA methylation analysis, single-cell sequencing, and spatial transcriptomics. We support projects from a range of materials, such as DNA and RNA of a range of qualities and quantities as well as tissue, plasma and cell specimens including infectious material. We are currently broadening the support for FFPE and fixed cells, as well as cell-free DNA. The platform is equipped to analyze very large numbers of samples with accredited pipelines, as well as cutting-edge genomic analyses with new methods.

The **Clinical Genomics platform** focuses specifically on supporting clinical and translational research, including studies with prospective patient recruitment and real-time analyses. Key technologies include short- and long-read sequencing, single-cell analysis, and ultrasensitive variant detection. These technologies are complemented with diagnostic and medical expertise, as well as assay development, bioinformatics and clinical decision support, enabling an end-to-end service from sample preparation to clinical interpretation. The platform continuously develops, adapts, validates and implements new technologies and applications for clinical research and healthcare, and also constitutes the technological backbone of Genomic Medicine Sweden.

The **Clinical Proteomics and Immunology platform** harbour a broad repertoire of technologies and instrumentation to support research and implementation of precision medicine: i) Prep-Labs equipped to handle clinical samples; ii) Phenotyping of humoral and cellular immune response by mass-cytometry, sensitive quantification of chemokines; cytokines and large-scale serology profiling; iii) Highly multiplexed affinity-based assays and high-resolution mass spectrometry for molecular profiling in biofluids, single cells and tissue biopsies; iv) Analysis of self-sampled specimens to facilitate health monitoring of individuals and populations; v) Protein structural characterization and subtyping to support design of new vaccines and drug targets.

The **Metabolomics platform** provides assays for comprehensive and high-throughput profiling or targeted metabolite analysis by mass spectrometry or NMR for applications in translational- and precision health. The Exposomics unit aims to discover, profile or quantify molecules from environmental exposures, including chemical pollutants. Both metabolomics and exposomics are applicable for observational studies or interventions. Machine learning tools and algorithms allow integration of metabolomics/exposomics data with other -omics layers and with clinical information to develop predictive models. Services target a broad range of precision medicine applications, including early risk prediction, prevention, and treatments to improve human health.

The **Spatial Biology platform** offers several methods applicable for future precision medicine: i) Highly multiplexed imaging enables staining for all relevant markers in one tissue slide for faster and more precise diagnosis of solid tumors. New promising markers can simultaneously be tested in trials for its clinical significance; ii) Global and targeted spatial transcriptomics allows for early detection of morphologically normal tissue regions, spatial distribution and clonal heterogeneity using large gene panels of prognostic and diagnostic value. iii) Untargeted and targeted spatial mass spectrometry for spatial information of small molecular weight species (signaling molecules, metabolites, lipids, peptides, proteins).

The **Cell and Molecular Imaging platform** is expanding clinical partnerships as well as sample and data handling tools to collect and process medical images. In one development project, the Cryo-EM unit aims to catalogue a patient's antibody epitope landscape in relation to specific infection or autoimmune responses. In the Integrated Microscopy Technologies unit, the Advanced Light Microscopy node is working with the Spatial Biology platform to build multiplexed proteomics analysis as a national service for clinical research. At newer nodes, technologies such as focused ion beam scanning electron microscopy and correlative array tomography offer 3D views of tissue and cell structures in complex or rare specimens, including clinical samples.

The **Integrated Structural Biology (ISB) platform** provides the following services for precision medicine: i) Screening of small molecule binding sites with atomic resolution; ii) Eptitope mapping of biotherapeutics; iii) De novo sequencing of antibodies; iv) Conformational dynamics and dynamics of protein-protein and protein-ligand interactions; v) Identification of constituents in large protein complexes; vi) Higher order structure (HOS) analysis of biologicals. These technologies generate static and dynamic knowledge on an atomic level that can be merged with big data in order to facilitate precision pharmacology and precision medicine. ISB is crucial for drug discovery and understanding the function of individual mutations and their pathology.

The **Chemical Biology and Genome Engineering platform** combines chemical, genetic and proteomic techniques to turn phenotypic observation into mechanistic insight. The following services are relevant for treatment guidance, biomarker identification or drug discovery: i) Access to known drugs and user-customized drug libraries; ii) Synthesis of drug-related chemotypes as controls; iii) Drug screens and profiling in close-to-patient cells and complex models; iv) CRISPR-based creation of cell models capturing specific mutations; v) Genetic screens and 2D proteomics profiling in primary cells and organoids; vi) Identification of targets, pathways and mechanisms of actions with functional genomics and chemical proteomics in a miniaturized format.

The **Drug Discovery and Development platform** aims to turn academic discoveries into innovations - prototype drugs - and to provide technologies and training for state-of-the-art drug discovery in Sweden. The platform offers i) expertise and support to promote progress of projects towards pre-clinical proof-of-concept and a strategy for further development; ii) consultation on requirements for precision medicine and implementation in drug discovery research; iii) identification of molecular binders (antibodies and small molecules) to protein targets. Therapeutic modalities supported include small molecules, antibodies and oligonucleotides, as well as novel modalities (e.g., cell therapies and proximity inducing agents).