Open for collaboration: an academic platform for drug discovery and development at SciLifeLab

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The Science for Life Laboratory Drug Discovery and Development (SciLifeLab DDD) platform reaches out to Swedish academia with an industry-standard infrastructure for academic drug discovery, supported by earmarked funds from the Swedish government. In this review, we describe the build-up and operation of the platform, and reflect on our first two years of operation, with the ambition to share learnings and best practice with academic drug discovery centers globally. We also discuss how the Swedish Teacher Exemption Law, an internationally unique aspect of the innovation system, has shaped the operation. Furthermore, we address how this investment in infrastructure and expertise can be utilized to facilitate international collaboration between academia and industry in the best interest of those ultimately benefiting the most from translational pharmaceutical research – the patients.

Swedish pharmaceutical industry and research

Being a small country with only 10 million inhabitants, Sweden has a proud history of successful organic growth of its pharmaceutical industry with companies such as Kabi [the first company to license Genentech's recombinant DNA technology later overtaken by Pharmacia (subsequently merging with Upjohn, and later being closed as a part of Pfizer)], Hässle (bought by Astra) and Astra (merged with Zeneca to form AstraZeneca). Even today, after the closure of three out of four major global pharma research sites located in Sweden, pharmaceuticals still represent one of Sweden's largest export products (a large part originating from AstraZenca's manufacturing plant in Södertälje). The aftermath of the industry's turbulent reorganization has created several geographical areas with strong life science innovation capacity [i.e. Stockholm/Uppsala (51% of life science companies), Malmö/Lund (19%) and Göteborg (17%)], hosting a plethora of smaller biotech companies (the largest now being Medivir outside Stockholm) [1].

Many of the products that became the cornerstones of the Swedish pharma and biotech industry (Macrodex®, Xylocain®, Seloken®, Healon®, Pulmicort®, Genotropin®, Losec®, Olysio®, among others) were based on discoveries made at, or in close collaboration with, academia [2]. In today's more fragmented industrial landscape there is a need for a new framework to capitalize on existing innovative research at universities, and to leverage projects with a capacity for generating new drug candidates. In the Research and Innovation Bill 2012, the Swedish Government allocated approximately US$6 million per year (2013–2016) to establish a drug discovery effort at the national Science for Life Laboratory (SciLifeLab) as one effort toward this goal. The aim was to build on Sweden's long tradition in drug development, and to expose academic drug discovery projects to opportunities for international collaborations, grants and investments.

SciLifeLab

SciLifeLab is a Swedish center for molecular biosciences with focus on health and environmental research [3–5]. The center combines frontline technical expertise with advanced knowledge

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GLOSSARY

ADME relates to a drugs – adsorption, distribution, metabolism and excretion.
CD candidate drug – the final product of the preclinical development of a pharmacological substance that has undergone regulatory safety studies that allows first-time-in-human dosing.
Hit2Lead the process of going from an initial validated chemical starting point 'hit', typically identified from a high-throughput screen, to a molecule with partially optimized properties for in vivo use (e.g. potency, solubility, metabolic stability, permeability, etc.).
SAR relates to how structural changes among a series of small molecule compounds effect potency, ADME and other properties of importance for a safe drug.
Screening cascade the iterative process by which a small molecule or biological therapeutic that meets the TPP will be optimized and identified.
TPP target product profile document tries to outline the desired properties of the proposed new drug already at the start of the project; two important questions to answer early on is how the proposed product will differentiate from current therapies and medical practice in a value-adding way and how preclinical results will be translated to a clinically measurable response.

of translational medicine and molecular bioscience. SciLifeLab, with two nodes, one in Uppsala and one in Stockholm, is a national resource hosted by four universities together: Karolinska Institutet, KTH Royal Institute of Technology, Stockholm University and Uppsala University. Researchers from all of Sweden can use the technology and the knowhow available at SciLifeLab. In addition, SciLifeLab aims to create a strong research community through workshops, seminars and courses. Users of technologies and expertise provided by SciLifeLab are found within academia, industry, authorities and healthcare. SciLifeLab also encourages partnerships and mediates collaborations between players in the life science sector.

SciLifeLab DDD platform and the objective of this article

SciLifeLab Drug Discovery and Development (SciLifeLab DDD) has been set up as a platform for early drug discovery and development and commenced its operation in early 2014. In this paper we discuss the platform as one of several possible ways to stimulate translational research. The SciLifeLab DDD mission is to help transfer basic research to early drug development programs, and to build an environment for scientific collaborations of international standard, competence and advanced infrastructure in the area of drug discovery. The platform offers intellectual and technical assistance to individual research groups with pharmaceutical projects. In addition, we strive to establish SciLifeLab DDD as a natural portal and collection point for Swedish academic drug discovery efforts. A further aim is to establish an attractive environment for collaboration between academia and industry in the context of SciLifeLab's overall mission. Herein, we present the infrastructure from an international perspective, and discuss how this national resource could help engage academic researchers more widely in private and public international initiatives aiming to bring new medicines to patients. We also reflect on lessons learned from our two first years of operation, with the hope that this will be useful to other new academic drug discovery centers being set up globally.

A changing role of academia in drug discovery and different 'business models' for academic drug discovery centers

The global pharmaceutical industry is currently undergoing a paradigm shift where more early drug research is done in collaboration with academia and through public–private partnerships [6]. The role of academia in the development of new drugs has been summarized [7–9], and these studies show that the most innovative drugs during the period 1998–2007 originated in academia and small biotech companies and not in the large pharmaceutical companies. Kneller's analysis [9] also showed a project flow from academia through small companies to large pharmaceutical companies for registration, approval and marketing. This clearly demonstrates the need for all these actors in the value-chain of drug discovery and development, and emphasizes academia as a vital initiator of successful drug discovery.

Many universities in the USA [10] and in Europe [11] have created units for academic drug discovery to take an active role in this changing landscape for pharmaceutical research. These new centers are important for coordination of activities, and are aimed at meeting the demand of a more active academia in bringing drug discovery projects toward the clinic. Several of these can be found through the organization AD2C (Academic Drug Discovery Consortium; http://www.addconsortium.org) [12]. For the purpose of comparison in this article, we selected a few international centers and grouped them into three broad categories (Table 1).

Investment-funded centers

Medical Research Council Technologies (MRCT), UK, Cancer Research Technology (CRT), UK, and Center for Drug Design and Discovery (CD3), Belgium, are examples of technology-transfer organizations from not-for-profit organizations with a clear aim to generate a return on investment for their organizations by licenses and royalties. MRCT and CRT have the rights to commercialize all projects supported by the Medical Research Council and the UK Cancer Research foundation, respectively. MRCT and CD3 originally focused on commercialization of internal research and technologies but now also make venture capital investments and seek external global opportunities for co-development. The strength of these centers is that they are self-sustained with strong funding from previous exits. They are role-models for commercialization of academic research with industry-standard business development function and resources and scope that are much larger than most academic drug discovery centers.

Alliance-funded centers

Max Planck Lead Discovery Center (LGC), Germany, Vanderbilt Center for Neuroscience Drug Discovery (VCNDD), USA, and RIKEN, Japan, are prominent examples of academic drug discovery centers with a clear mission to set up and commercialize drug discovery programs originating from within the Max Planck society, Vanderbilt and RIKEN, respectively. These centers typically

TABLE 1

Categorization of international academic drug discovery centers

Center type	Example	Strengths	Budget/FTEs
Investment-funded centers	MRCT (UK), CRT (UK), CD3 (Belgium)	Strong funding, self sustainable, industry-standard business development	MRCT: 130 FTEs CRT: £350 million per year CD3: €24 million fund
Alliance-funded centers	LGC (Germany), VCNDD (USA), RIKEN DD (Japan)	Industry funding of program, commercial interest secured	Project-specific – industrial rate
Research-funded centers	Broad (USA), DDU (UK), EIDD (USA)	Science driven, follow academic funding	Project-specific – depends on grants

Abbreviations: CD3, Center for Drug Design and Discovery; CRT, Cancer Research Technology; DDU, Drug Discovery Unit University of Dundee; EIDD, Emory Institute for Drug Development; LGC, Max Planck Lead Discovery Center; MRCT, Medical Research Council Technologies; VCNDD, Vanderbilt Center for Neuroscience Drug Discovery.

form an alliance with a large pharma organization for each individual program, and that organization then funds the further development of the program (up to clinical trials or beyond) within the academic organization. The strength of this model is that it opens a new funding stream and assures a commercial interest of the final product early on.

Research-funded centers

Broad Center for the Development of Therapeutics, USA, the Drug Discovery Unit at the University of Dundee (DDU), UK, and Emory Institute for Drug Development (EIDD), USA, are examples of centers that combine a core funding with research funding for an individual program from more-traditional academic funding organizations (e.g. Wellcome trust and Bill & Melinda Gates Foundation). Often, these actors have a strong support network to work on a dedicated disease focus (i.e. tropical diseases at DDU and viral disease at EIDD). The strength of this approach is that it is driven primarily by scientific excellence and reflects the academic funding to an individual principal investigator (PI) or disease area.

Although some organizations are well funded from a combination of core funding, grants and alliances, it is still reasonable to ask why these relatively modest investments in academic drug discovery would be successful when the global pharmaceutical industry, despite billions of dollars of investments, fails to deliver new products at a pace that satisfies unmet medical needs and shareholders' expectations [6,13,14]. We believe that the key for success is to identify, and interact closely with, researchers conducting cutting-edge biological research, where academic and industrial drug discovery programs are built but lack the knowledge or resources to bring discoveries to the patients. In addition, rather than taking over the researchers' project, we believe that working together with scientists to translate their discoveries toward true patient benefit would be more efficient and rewarding for both parties. Academic scientists in general are not trained in drug discovery and an independent group of professional drug hunters could help to clarify important factors for progression of projects into clinical studies and add the needed technical drug discovery knowhow into the existing academic community.

Considerations for establishing an academic drug discovery platform in Sweden

The Teacher Exemption Law, unique to Sweden, influenced our planning and ways of working at SciLifeLab DDD. This law states that the individual scientist, not the university, owns their discoveries and it allows them to commercialize discoveries made from publicly funded research and thereby be personally accountable for any financial risk and reward during this process. The main objective of SciLifeLab DDD is to be a facilitator for Swedish academic researchers to bring their basic biological discoveries toward patient benefit. The ultimate goal is to provide more clinical candidates for further studies in humans, but realistically such a goal is associated with a very high risk in the long-term, because it requires investment of hundreds of millions of dollars and 6–7 years of development. Both these aspects made us decide to focus our assistance early in the value chain of a drug project. Later parts, which require greater capital and longer time-lines, are better done with a shared risk or reward from private and public funds. Moreover, SciLifeLab DDD is an academic activity hosted by four universities. As such, the guiding principle should be based on academia's missions: research, education and interaction with the surrounding society (in particular industry and healthcare). When a drug discovery project becomes commercially viable, it needs to seek funding from other sources than those financing basic research.

By acting in the early phase of drug discovery, SciLifeLab DDD also avoids competition with companies specializing in contract research services. Instead, it is anticipated that, by emphasizing the quality of data required for a drug discovery project to attract seed investments for continued development, the service and competence that are offered through consultants and contract laboratories become more visible to the start-up and academic community. Thus, it is anticipated that a virtual company model, similar to the alliance-funded centers concept, could emerge after the involvement of SciLifeLab DDD. In addition, there are other tools in place in the Swedish innovation system for later phase projects sponsored by Vinnova – the Swedish innovation agency.

How to secure commercial interest at the receiving end

At the front end of the drug discovery value chain is basic academic research that emerges from the large-scale platforms within the national SciLifeLab, for example the National Genomics Infrastructure [15] and the Chemical Biology Consortium Sweden [16]. These contributors strengthen target identification and validation through genomic sequencing and screening for tool compounds, respectively. The focus of SciLifeLab DDD will therefore be to assist projects that have a defined rationale for a drug discovery program up to a point where the project has matured enough to be of interest for commercial partners or granting agencies specializing in commercialization of projects. Our place in the value chain should be viewed such that the final product from SciLifeLab DDD

is a proprietary small molecule or a human protein drug with preclinical efficacy in an appropriate model(s) with translational values that support further development to clinical proof-of-concept studies.

However, animal data alone is rarely enough to attract a potential commercial partner [17]. Many academic publications already contain data from animal studies; but all too often such studies have been done with known compounds and lack information on fundamental compound properties such as solubility, permeability, metabolism, dose–response, exposure, among others. Moreover, even basic views on how to bridge the laboratory-controlled conditions in which the compound is active in animal models to the complex situation in addressing human disease might be lacking. To be of interest to commercial partners it is important to have a clear understanding of future medical needs, a reasonable rationale arguing for why the particular drug should be efficacious in a specific category of patients, an analysis of the competitive situation and not least an appreciation of which skills and strategies are needed later in the development phase. To be successful, early academic drug discovery projects also benefit from a clear strategy for further preclinical and clinical development [i.e. a target product profile (TPP) including a draft translational science plan (Fig. 1)].

Organization of SciLifeLab DDD

At the outset, we decided that SciLifeLab DDD should be set up to support small molecule and protein therapeutics drug discovery programs. The rationale for including both being that the Chemical Biology Consortium Sweden, offering services for explorative high-throughput screening to find chemical tools [16], was already in place, as well as the collected knowhow around antibody development originating from the Human Protein Atlas [18]. Given that SciLifeLab DDD should be open to accept project proposals from all disease areas, we needed to build a generic internal drug discovery engine, and rely on the project owner for in-depth understanding of the biology and expertise in related *in vivo* models. The platform thus has nine units, termed facilities (Fig. 2). These are stationed at the SciLifeLab premises in Stockholm and Uppsala (from February 2016, the human antibody therapeutics facility expanded its operation to Lund University) but interact with researchers throughout the country for the projects.

The compound handling and IT infrastructure facility works together with the Chemical Biology Consortium Sweden [16] and has access to approximately 200,000 chemical substances. The unit offers substance handling and sends assay-ready plates across the country. The group is also working to establish a national IT infrastructure to store information about the biological properties of the compounds that would allow easy access for the project owner. The protein expression and characterization facility provides recombinant proteins from bacterial, insect and human cells for drug discovery projects. The facility for biochemical and cellular screening has industry-standard robotics for conducting pharmacological assays of compounds and proteins in plate formats. Medicinal chemistry Hit2Lead (see Glossary) and lead ID offer expertise in medicinal and computational chemistry for synthesis of new drug candidates, and the biophysical screening and characterization facility uses biophysical methods like surface plasmon resonance (SPR) biosensor technology and structural biology to characterize the binding of ligand and target protein. The ADME group is part of Uppsala University Drug Optimization and Pharmaceutical Profiling Platform (UDOPP) [19] and investigates *in vitro* pharmacokinetic properties of drug candidates, *in vivo* exposure and assists with early metabolic profiling. The *in vitro* and systems pharmacology facility makes detailed mechanistic studies of a substance mechanism of action and has access to patient-derived cells for profiling. The human antibody therapeutics facility offers selection, characterization and development of human

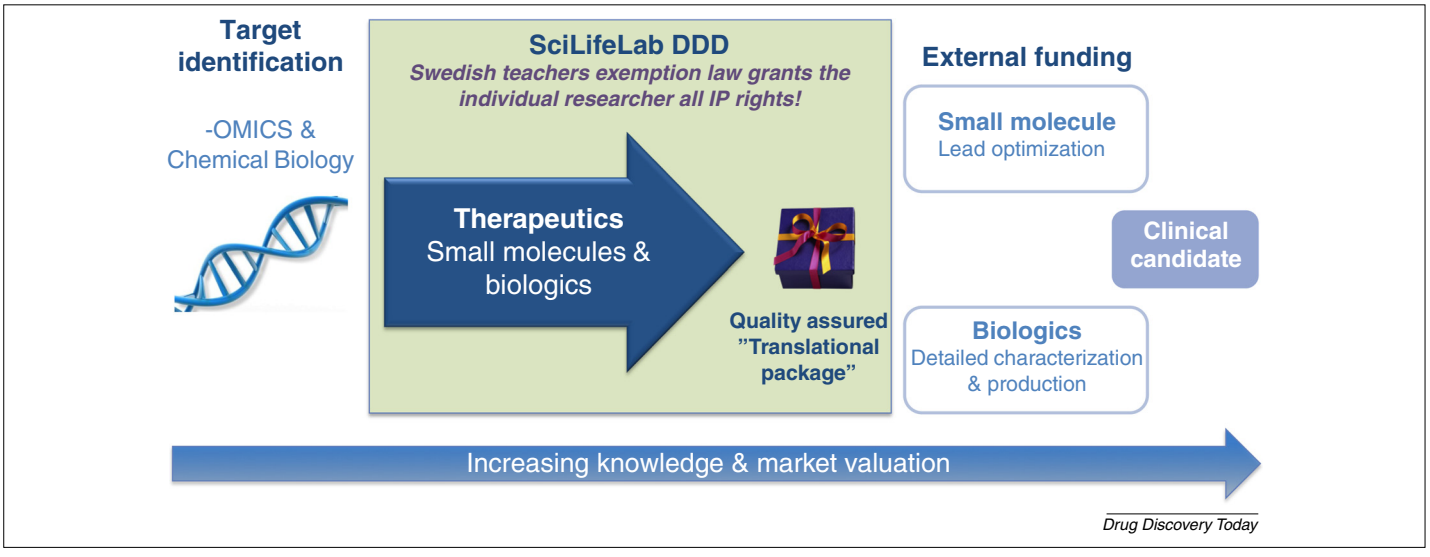

FIGURE 1

The role of SciLifeLab Drug Discovery and Development (SciLifeLab DDD) platform is to translate basic biomedical research to a point where projects are mature enough to seek external funding or commercial partnerships. This is accomplished by offering granted projects access to technical service and intellectual expertise in drug discovery and development. According to the Swedish Teacher Exemption Law, researchers have the right to commercialize the results of their research – no intellectual property (IP) ownership is therefore assigned to SciLifeLab DDD.

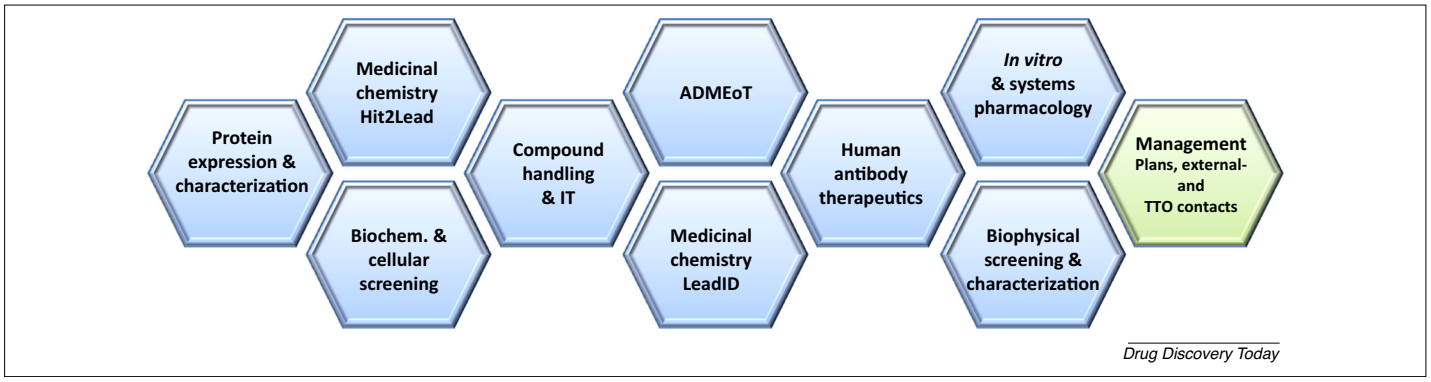

FIGURE 2

SciLifeLab Drug Discovery and Development (SciLifeLab DDD) is organized in nine facilities and one management team. The nine facilities offer industry-standard infrastructure and expertise for academic drug discovery projects. The management team offers strategic advice and support to scientists and innovation offices in preparing target product profiles and plans for drug discovery projects.

antibody drugs through intellectual property (IP)-free phage libraries. A total of 36 fully dedicated full-time employees (FTEs) at the facilities are currently engaged in the work at the platform.

An international comparison, through a search in the AD2C database, reveals that globally only a few centers offer a combination of small molecule and antibody based drug discovery capability. Likewise, ADME and systems pharmacology are capabilities that are less common to the majority of academic drug discovery centers. Starting in 2016, we also include drug safety assessment capabilities within the platform; thereby, we will be able to make an early assessment of the potential liabilities associated with manipulation of the biological target of interest.

The facilities are each led by a head of facility. The platform as a whole has two full-time directors leading the work in Stockholm and Uppsala, respectively, and one project coordinator and, through a strategic collaboration with the national center for toxicological sciences SweTox, a drug discovery toxicologist. The management team leads the overall activities of the platform. This team also offers strategic advice and support to scientists and innovation offices in preparing target product profiles and plans for drug discovery projects. All the staff at the facilities work full-time with the drug discovery projects within the platform. Twelve professors at the host universities support projects with their experience and assure that the facilities maintain the highest scientific quality (e.g. with regard to technology development they conduct their research separately from the facilities). The directors, heads of facility and the professors make up the platform leadership team, and report to an external platform steering group, responsible for overall strategy and, most importantly, project prioritization.

Collectively, the SciLifeLab DDD staff have more than 250 years of industrial experience in drug development gathered from more than 15 different pharmaceutical companies. Furthermore, the staff and associated professors have experience from starting some 20 new companies; thus being able to offer valuable advice for those researchers who wish to develop their drug projects further through a separate company; with the Swedish Teacher Exemption Law, initiation of a start-up company to hold IP rights is often required, even for projects seeking early licensing to a larger company.

Project model

SciLifeLab DDD is a resource for all academic researchers with an ambition to participate in drug development of small molecule and protein therapeutics. This means that the platform has to accommodate proposals from all kinds of disease areas and that the specific biological knowledge and disease models need to be available from the academic researcher or through their collaborators. This generality is different from some of the international centers listed above, which focus on particular therapeutic areas.

To secure transparency and thorough evaluation, an external platform steering group composed of experts within clinical medicine, financing and pharmaceutical industry prioritizes between the projects. A successful project needs to offer solutions for a medical need, have a good rationale for the therapeutic mechanism of action, present an advantage over any identified competitors and be positively evaluated on several other parameters (Fig. 3). The project must also be feasible within the financial

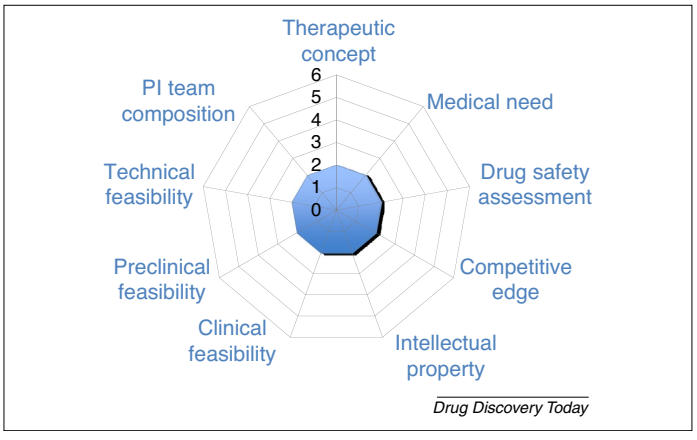

FIGURE 3

The assessment of an academic project's potential as a drug discovery project needs to include other factors than those traditionally used for evaluating proposals submitted to funding agencies. Shown is the set of criteria currently used by the platform steering group for project prioritization. Competitive edge (differentiation) is the largest hurdle and needs to be objectively assessed using professional competitive intelligence databases and a continuous industry dialogue.

framework needed for a preclinical proof-of-concept and the funding it hopes to attract to pursue the project further. Researchers apply for entry to the platform and, following a favorable evaluation, SciLifeLab DDD provides the granted projects full access to the infrastructure in the form of instrumentation, facilities and personnel and the fee for the researcher is limited to the cost of consumables.

During the course of a project, members from SciLifeLab DDD and the research group jointly work on drug project, which becomes a highly interdisciplinary endeavor. The core of the drug discovery project at this stage is centered on the screening cascade in the TPP (Fig. 4a). The screening cascade is the roadmap that, already at the start of the project, outlines how an active small molecule or antibody therapeutic with the requirements in the TPP will be identified. All activities needed at the various facilities are coordinated by the assigned SciLifeLab DDD project leader according to a detailed Gantt chart (Fig. 4b) that spans a six-month period. The steering board assigns priority to individual projects and activities for 6 months, after which the project is subjected to new evaluation in competition with new project proposals. Thus, it is essential to define clear short-term stop–go decisions and deliverables for a particular 6-month period so that each cycle adds value to the project and allows the project to be progressed in the PI group if priority would decrease for the next cycle.

During the manning of the infrastructure we strived to recruit individuals with experience from industrial drug development. The research group is responsible for continued evolution of the biology and for liaising with innovation offices, and future external parties; however, we noted a large demand for assistance with external interactions from our collaborating researchers, which will demand a slight modification of our model (*vide infra*). Originally, we planned to support three full-size small molecule and three biopharmaceutical projects running in parallel, but a high demand on our services, and more-efficient use of available resources, allowed us to increase the number of supported drug discovery programs to 10–12 projects run in parallel. To fully optimize the capacity of the platform and balance workload, smaller service projects (i.e. requesting limited support from only one facility) can be supported provided that they do not interfere with prioritized programs.

Identifying academic research with potential for drug development

Researchers interested in the service of SciLifeLab DDD are invited to make contact for a first unconditional consultation. Such meetings can be initiated by the individual researcher but we also spend considerable time and effort to make ourselves known to Swedish academics by hosting events and personal meetings at various

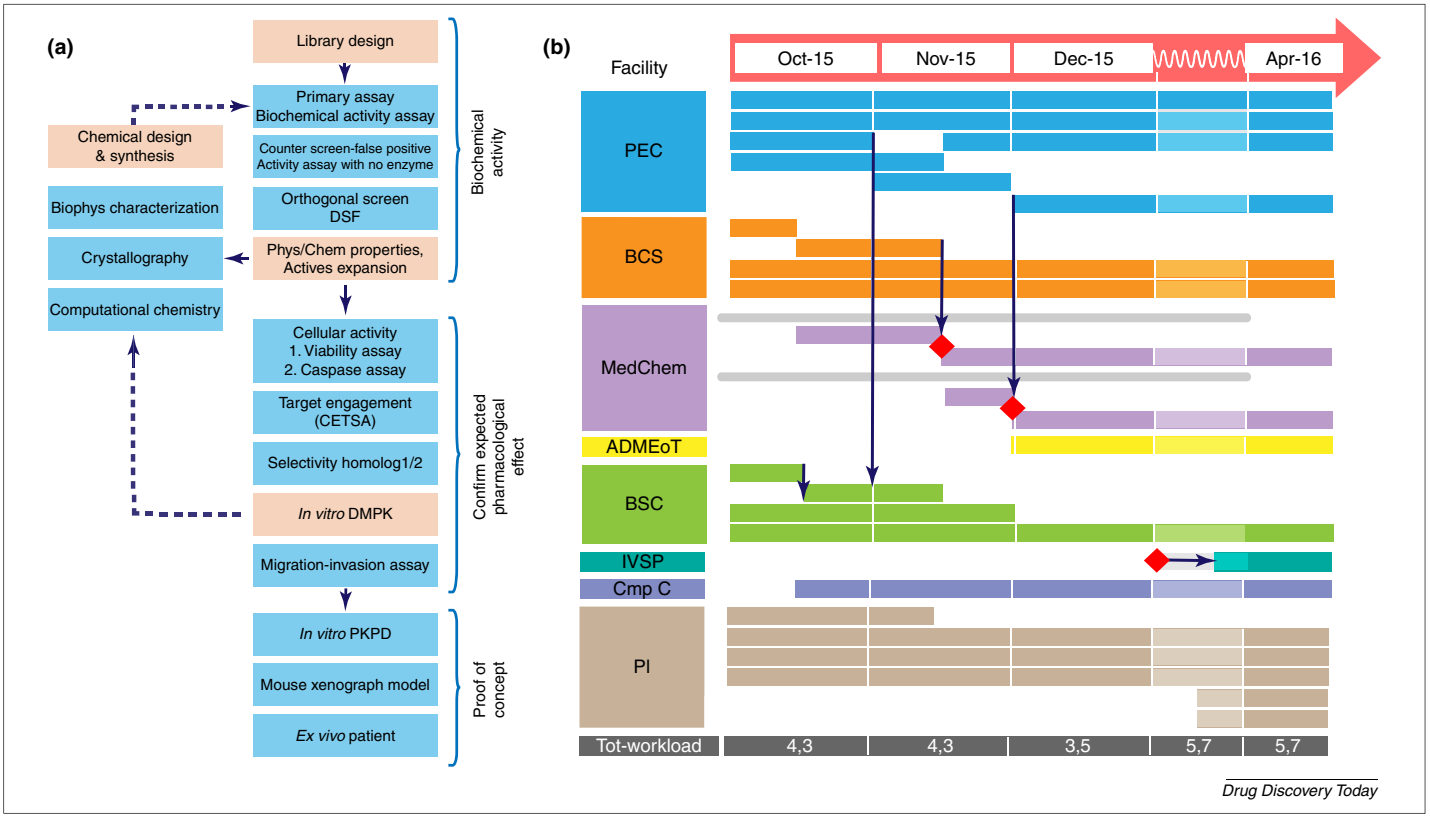

FIGURE 4

(a) Example of a representative screening cascade for a small molecule oncology project. The screening cascade is the roadmap to optimize and identify a small molecule or biological therapeutic that meets the target product profile (TPP). **(b)** Representative Gantt chart demonstrating the highly cross-functional project work ongoing at the facilities for a small molecule drug discovery project in the early stage of Hit2Lead generation. See text for explanation of facility (team) competences, that is, PEC, protein expression and characterization; BCS, biochemical and cellular screening; MedChem, medicinal chemistry Hit2Lead, ADMEoT ADME and Toxicology; BSC, biophysical screening and characterization; IVSP, in vitro and systems pharmacology; Cmd, C compound center; PI, resources from the principal investigators own laboratory (not accounted in the Gantt).

university locations around Sweden, by attending scientific meetings and by working with the members of the innovation system and funding agencies. The universities' innovation offices have proven to be a good channel to identify researchers with promising projects. The innovation officers at the different universities often have a good overview of which projects at their university are in line with our mission. SciLifeLab DDD has the expertise and experimental resources that are often needed to identify and fill the gaps in promising early drug discovery projects identified by the innovation offices. Innovation offices have access to complementary resources (e.g. patent attorneys and business development capabilities that are essential for drug discovery projects). Close collaboration with the universities' innovation offices is therefore instrumental for the SciLifeLab DDD operation.

SciLifeLab DDD aims to offer the researchers a useful, confidential opinion of their project's advantages and disadvantages from a drug discovery perspective. This feedback should also prove valuable to project proposals that are not prioritized by the platform steering group. Indeed, many researchers testify that a first informal meeting with SciLifeLab DDD has led to improvement of their regular funding applications. DDD assures that all shared information is treated as confidential. If a project is considered to be competitive, SciLifeLab DDD assigns one of the DDD directors as a pre-project leader for the project to work together with the research group to put together a full project proposal for further assessment by the steering group. Some limited wet-lab activities might take place during the pre-project phase (e.g. druggability assessment and *in vitro* ADME profiling of tool compounds).

Owing to the highly cross-functional nature of drug discovery, multiple interactions between the research group and SciLifeLab DDD are needed to prepare the project before prioritization to clarify project goals and to make plans. Researchers testify that these TPPs and accompanying plans are of great value, even if the steering group does not prioritize the project. We have changed our operating model somewhat during the second year, and now offer our support to bring forward TPPs for projects seeking alternative funding or ways to progress their drug discovery program, and these plans are viewed as distinct deliverables from the DDD platform.

Leveraging a national platform with international collaboration and innovation

How can the Swedish Government's investment in a national infrastructure with industry-standard equipment and expertise best serve its purpose? We believe that, on top of the projects we have capacity to handle internally, we need to offer additional value to the academic drug discovery community (e.g. by facilitating international efforts).

International public–private collaborations

One opportunity to add additional value beyond the internal project work is to utilize the infrastructure investment to help Swedish researchers participate in international collaborations, such as the EU's Horizon 2020 and the Innovative Medicines Initiative (IMI). This is exemplified by the *in vitro* ADME profiling facility at SciLifeLab DDD participating in the IMI program ENABLE, which aims to develop new antibacterial agents [20], and the Human Antibody Therapeutics Facility taking part in the new IMI program ULTRA-DD coordinated by Novartis and The Structural Genomics Consortium [21]. In these cases, the instrumental throughput is not yet limiting (although it will be eventually), meaning that such collaborative projects can be harbored, provided external funds are available to cover additional personnel, rent, among others. SciLifeLab DDD could be effectively utilized for coordination of new international multicenter projects (e.g. IT and substance management).

Academic interactions with open innovation initiatives

In addition to taking part in international public–private collaborations, SciLifeLab DDD should strive to represent a link between Swedish academic research in the drug discovery area and the global pharmaceutical industry. Most large global pharmaceutical companies offer an open innovation model for collaborative early drug discovery projects. This should provide an opportunity to establish fruitful exchange and collaborations with the global pharmaceutical industry that covers all of Swedish academia. Given the Swedish Teacher Exemption Law, many academics in Sweden might prefer to apply to an organization that does not place any restriction on future license or ownership, because the open innovation calls offered by the pharmaceutical industry usually entail some IP restrictions. Other scientists might prefer to interact directly with a pharmaceutical company. We see an opportunity for project proposals that have been prepared with the input from industry-trained professionals at SciLifeLab DDD to be more competitive in the global industrial open innovation system. These projects have been pre-screened at a national level, the researchers have been prepared for the demands put forward on a project by industry and they will better understand the financial value and risk of a project after being evaluated at SciLifeLab DDD. Clearly, this represents a value that should be a win–win opportunity for further interactions between the individual researcher, SciLifeLab DDD, and the global industrial open innovation system.

Reflections from 2 years of operation

Reflecting on our first 2 years of operation, we believe that we have shared, and attempted to mitigate, many of the obstacles and recommendations put forward in the excellent paper by Dahlin *et al.* [22]. Below, we summarize our own experiences.

Need for dialogue and knowledge transfer

Maybe not unexpectedly, we have experienced something of a 'cultural clash' between purely academic investigator-initiated research, where the main deliverable is publications in high-impact journals, and, by contrast, the specific requirements for drug discovery. The foundation for academic drug discovery is based on scientific discoveries that in most cases have not been initiated with drug discovery as a downstream aim. However, once the decision is made to bring forward a compound and a translational package of validated data supporting the target hypothesis, one enters a stage where experiments are planned to reach specific conclusions and to meet precise milestones. To use limited resources efficiently, the SciLifeLab DDD platform needs to challenge projects and define clear stop–go criteria for further engagement. These strict requirements can sometimes be difficult to accept for academic researchers who are exposed to the industrial

way of thinking for the first time. To leverage these two ways of conducting research and development, we believe that undergraduate and graduate training should include innovation and drug discovery whenever appropriate. A graduate school in drug discovery is already in place [23], and exchange between companies and universities in the form of shared PhD students or postdocs should be further encouraged.

Proposals to SciLifeLab DDD span project ideas emerging from early basic research to projects almost ready to enter clinical studies. Irrespective of background, our experience is that several project proposals are not considered appropriate for the platform as a result of lack of industrial competitiveness. Most principal investigators we meet are internationally renowned and well funded by national and international funding agencies. They are aware of all the important academic competition, but less often they follow the work that has been conducted in industry (i.e. data reported in the patent literature or through other channels of information). On multiple occasions we have been able to identify that there are several compounds marketed, or in late-stage clinical trials, for the same target or mechanism as the researchers describe as novel. To assure a holistic view of the target and the disease landscape as a whole an unbiased literature search in commercial databases such as Thomson Integrity®, Citeline® or similar is required. We thus conclude that the academic medical research community that aims to search for new therapies would benefit from a broader knowledge base when designing new projects.

Understandably, there is also limited knowledge in the academic community about the extent of work, data and investments required to bring new medicines to patients. These aspects need to be considered from the very beginning when new active compounds or biologics are identified in assays by screening or selection. Ultimately, a potential new candidate drug's differentiation versus current treatments and compounds should be demonstrated against major competitor compounds and drugs on the market. Data supporting differentiation of the final product and feasibility to conduct conclusive clinical studies are essential to justify and attract the billions of dollars of investments that are required to bring the project to the market and clinical practice.

In addition to the intellectual and practical services above, we strive to establish SciLifeLab DDD as the natural portal for Swedish academic drug discovery efforts. This means reaching out to the broader community of life science actors (e.g. innovation offices, translational and clinical research centers, funding agencies, industry, consultants, students, politicians, among others). To unite and cover the interest of so many stakeholders, we recently started a newsletter [24]. We also organize two mini-symposiums related to DDD every year. We find that coaching, during individual meetings and through workshops and conferences, is required to raise awareness around these subjects to make academic drug discovery more successful.

Technical assessment of project quality

An important task for the SciLifeLab DDD platform is to make a fair assessment of the quality of the project based on the available data generated from the principal investigator's own laboratory (i.e. the transfer of experimental data from a research laboratory to the platform). The high degree of irreproducibility of complex biological systems that has been the focus of intense debate recently [25–27] makes this a challenge. In addition, there is a risk that projects are based on results that originate from assay artifacts caused by chemical pan-assay interference compounds (PAINS) [28] in commercial chemical libraries or through a non-validated and quality controlled assay. We have therefore established an initial project period in which we establish crucial assays in the proposed screening cascade at the SciLifeLab DDD platform to avoid, to the best of our ability, these pitfalls. It has also proven vital to have in-house access to the primary SAR driving assays because the academic research group, owing to other engagements, projects and limited resources, cannot always prioritize these collaborative efforts.

One probable factor contributing to the limited reproducibility of preclinical *in vivo* studies is the lack of exposure analysis. Many published animal studies report effect as a function of dose, without documented knowledge of plasma exposure *in vivo*. By offering access to bioanalysis of small and large molecules through our ADME facility we hope to increase the quality of the drug discovery projects. We suggest that reproducibility of biological studies could be improved if editors of leading journals encourage that the actual concentration of the substance in plasma is reported for *in vivo* results.

Strategies for further development and the Swedish Teacher Exemption Law

The Swedish Teacher Exemption Law adds a dimension of complexity to the way projects proceed after exiting the SciLifeLab DDD platform. As personally being the owner of all IP and data generated throughout the research project, an academic scientist in Sweden is in a unique position to decide on how to proceed with the project (e.g. apply for continued public funding, apply for private funding within open innovation, license the program to an industrial partner or form a start-up company). These different paths require vastly different investment in terms of time, engagement, funding and IP strategy, to name but a few variables. We experience that researchers, often finding themselves in this position for the first time, are perplexed by the multitude of options, which calls for an independent speaking partner for these considerations. Specialized structures at the Swedish universities, such as innovation offices and holding companies should ideally be best suited to handle such dialogues with an individual and give advice on how a project should proceed. In a workshop held together with these organizations in Sweden last year the specific challenges associated with the exit phase of a particular academic drug discovery project were addressed.

SciLifeLab DDD strives to facilitate this transition by frontloading the exit phase with close interactions with the university innovation systems and by incorporating the researcher's preferred exit strategy in the plans so that compounds with the right characteristics are identified as early as possible. Nevertheless, we foresee a potential liability that academic drug discovery projects might not reach further development because of difficulties in mobilizing the right expertise and resources to assure a commercially viable continuation of the project. The Swedish Teacher Exemption Law stimulates the entrepreneurship among scientists at universities to bring their basic scientific discoveries toward commercialization, and contributes to the Swedish innovation

landscape. However, the Swedish Teacher Exemption Law also reduces the mandate of universities to make the best deal possible for the results generated within a project. In this context, it is important to remember that the scientist, being owner of their invention, could have special preferences for how to progress their project. Through active collaborative work, we believe that SciLifeLab DDD can take an important role in driving a constructive and pragmatic dialogue between the research scientist and the university innovation systems to find solutions for how to deliver commercially attractive drug projects for further progress into the clinic.

Drug repurposing: a 'free' opportunity for the global pharmaceutical industry

Despite the limited time-frame in which the SciLifeLab DDD platform has operated, we can conclude that many academic drug discovery projects identify new and unexpected biological activity of known drugs (i.e. by screening commercial sets like the Prestwick Chemical Library® in ingenious cellular models of human disease). This observation should be an encouragement for those pharmaceutical companies that have shared their collections of (closed) clinical compounds with academic drug discovery centers, because the originator might still uphold patent protection for such compounds. Likewise, such drug repurposing should be highly beneficial for the patients because of shorter development cycles. However, there is a risk that the uncertainty associated with the patents, or perhaps inexperience on use-patent filing, licensing and prosecution from all those involved, would exclude much promising biology to be developed into human therapies. Typically, these results instead end up in publications without patent protection, thereby prohibiting further development by the discoverer of the new use or the original license holder. Sharing best practice of successful repurposing experiences [including IP rights (IPR) and licensing terms] will hopefully remove some of the uncertainties associated with this promising approach in the future [29].

Concluding remarks

The objective of this article is to highlight the DDD platform within SciLifeLab as the Swedish center for academic drug discovery. We have described our mission and objectives within Sweden's rather unique academic innovation system, characterized by the Teacher Exemption Law that gives Swedish academic researchers the right to personally commercialize their discoveries. We have also aimed to share our experiences in the hope that other emerging centers could benefit from our ongoing learning on how to gain the maximum output from the means at hand. Most importantly, we signal not only our role as the Swedish powerhouse for academic drug discovery but also our long-term ambition to use resources and expertise in international collaborations within public and private partnerships, recently exemplified through the IMI programs ENABLE and ULTRA-DD. We believe that an open climate that allows sharing of physical entities such as compounds, data and other resources as well as experiences and best practices, between academic and industrial partners, will be a prerequisite to increase the efficiency by which society and industry bring new treatment to patients who urgently need remedies for their ailments.

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