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International networks and funding opportunities for research in the field of rare diseases

non-exhaustive overview

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I. Preface

This paper summarizes existing international networks and funding structures in the field of rare diseases. It was established within the framework of Working Package 5 ("International Networking") of the National Concept on Rare Diseases (RD) under the co-lead of the Federal Office of Public Health (FOPH) and the State Secretariat for Education, Research and Innovation (SERI)

After conducting a survey in 2018 (here after: "Survey 2018") to assess the state of the international networking among Swiss RD experts, the Working group WP5 decided to list the existing networking and funding possibilities outside the European Reference Networks. Indeed, the Survey 2018 revealed that there is a rather limited use of international or foreign grants by Swiss experts. Although the majority of respondents to the Survey 2018 considered international collaboration as being positive and saw many benefits resulting from it, less than a third of all respondents declared having undertaken concrete steps to establish cooperation beyond their existing – mostly personal and not institutional - partnerships.

Thus, there is a need to improve stakeholder awareness regarding access to international networks and funding structures.

In the FOPH/SERI Survey 2018, most of the relevant international partners mentioned by the experts were individual experts, hospitals and care institutions coming from different EU member states and from countries outside the EU. Other foundations or international networks were barely mentioned. A considerable number of respondents specifically indicated the wish to gain access to the European Reference Networks (ERN). The FOPH and the SERI have written a factsheet on this topic explaining the current situation concerning such access (an up-dated version of the factsheet will be available on the FOPH website in April 2021). Indeed, Switzerland does not apply the EU Directive 2010/24/UE on cross-border health care establishing the ERNs at the EU level. Therefore, it is not currently possible for Swiss institutions to be part of the ERNs. The FOPH continues to follow the developments on this topic. For the time being, this paper does not address the question of access to ERN.

Finally, even though patient organizations also contribute to the funding of RD Research work and initiatives, we only mention the three largest organizations at the end of the document. The Orphanet database (see below) or on the ProRaris website provide a more comprehensive list of patient organizations and networks.

II. Existing international (expert) networks

Besides the European Reference Networks (ERN) (see above), there are many other international or country-specific networks involved in the field of rare diseases or in related areas. Even if they are limited to national experts or institutions, they publish useful information on ongoing research. Here are a few examples of European networks and other important networks outside Europe (**Attention**: Funding

structures and opportunities as well as research institutions are listed under Chapter III):

1) **Orphanet** is an international reference portal for rare diseases. Orphanet was established in France by the INSERM (French National Institute for Health and Medical Research) in 1997.This initiative became a European endeavor from 2000, supported by grants from the European Commission (RD-Action - see below): Orphanet has gradually grown to a consortium of 40 countries, within Europe and across the globe (including Switzerland). Orphanet provides high-quality information on rare diseases, and ensures equal access to knowledge for all stakeholders. Orphanet also maintains the Orphanet rare disease nomenclature (ORPHAnumber), essential in improving the visibility of rare diseases in health and research information systems. Swiss Orphanet is based in the Geneva University Hospitals.

2) **European Network of Resource Centres for Rare Diseases** (RareResourceNet) aims at accelerating the development and the implementation of holistic high quality care pathways for people living with a rare disease across Europe, to contribute to raise standards of care and support. RareResourceNet was created within the INNOVCare project. The gathering of services in this network is possible following the mapping of specialized social services for rare diseases performed within the European Joint Action for Rare Diseases (EURCERD Joint-Action, 2012-2015).

3) **Rare Diseases Clinical Research Network (RDCRN)** is a non-profit organization founded by the US National Institutes of Health (NIH) and the Office for Rare Diseases Research (ORDR) in 2003 and the program is now coordinated by the National Center for Advancing Translational Sciences (NCATS). Their aim is to contribute to the research and treatment of rare diseases and clinical outcome, while also encouraging the development of new approaches to diagnosis, prevention and treatment. The RDCRN consists of 20 distinct clinical research consortia with a Data Management and Coordinating Center (RDCRN). The consortia supports a broad range of clinical research, including clinical trials.

4) Another important network founded by the US NIH Common Fund is the **NIH Rare Disease Undiagnosed Diseases Network (UDN).** UDN is a research study to improve the level of diagnosis of rare and undiagnosed conditions. The UDN has established a nationwide network made up of a Coordinating Center (based at the Department of Biomedical Informatics at Harvard Medical School), Clinical Sites located in 12 cities across the United States and Core Facilities.

5) The **Rare Diseases (RDs) Global Open FAIR Implementation Network** (**RDs GO FAIR**) is a bottom-up, stakeholder-driven and self-governed initiative which aims to implement the FAIR data principles, making data findable, accessible, interoperable and reusable. Supporting the goals of the international rare diseases research consortium (IRDiRC – see below), the main purpose of RDs GO FAIR is to establish a culture in the RD community where members help each other choose, adopt, and tailor guidelines, standards, and tools to implement FAIR principles. It offers an open ecosystem for individuals, institutions and organizations working together through Implementation Networks (INs).

6) **The European Rare Disease Models & Mechanisms Network (RDMM-Europe)** was established by **Solve-RD** – an EU-funded (Horizon 2020) research project (see under). The overall aim is to boost research in rare diseases, discover new disease-causing genes and obtain evidence for pathogenicity through functional validation. Other similar networks can be found in other continents: For example, the Canadian **Rare Diseases: Models & Mechanisms Network** is a Canadian network established to catalyze connections between people discovering new genes in patients with rare diseases, and basic scientists who can analyze equivalent genes and pathways in model organisms.

7) **Asia-Pacific Economic Cooperation (APEC) Rare Disease Network (RDN):** APEC members share best practices and policies for addressing rare diseases and collaborate on the development of an APEC Action Plan on Rare Diseases. APEC Policy Dialogues bring together government agencies overseeing health and social services, academic experts from universities and teaching hospitals, industry executives and civil society, including patient groups.

8) **International Conference on Rare Diseases & Orphan Drugs (ICORD)** is an International Society for all individuals actively involved in rare diseases and/or orphan drugs, including health care, research, academic, industry, patient organizations, regulatory authorities, health authorities, and public policy professionals.

9) **Drug Information Association (DIA)** DIA's members come together to collaborate and problem-solve, discussing global and local challenges facing the life sciences field in an increasingly more

complex and interconnected world. DIA's goal is for this collaboration to result in better policies, regulations, science, research and development, and ultimately better patient outcomes worldwide.

III. Existing funding structures / Grant opportunities

Most scientific health research is funded by government grants, companies doing research and development, and non-profit foundations[1]. Thus, we have classified the existing funding structures for research projects in the field of rare diseases, including biomedical research with implications for RD research, into the following categories:

A) National (public) funding agencies and university research funding

B) International and EU funding structures (incl. Horizon 2020/Horizon Europe grants and Interreg projects)

C) Foundations and philanthropic funders, private research institutes, pharmaceutical companies grants and fellowships

D) Main patient advocacy groups with research grants and fund raising activities

A) NATIONAL (PUBLIC) FUNDING AGENCIES AND UNIVERSITY RESEARCH FUNDING

In a 2010 *E-Rare Survey on Rare disease research funding*[2], several national agencies, such as the US NIH, the French ANR and the UK NIH, stood out from the rest by allocating substantial resources for rare diseases research. The **Swiss National Science Foundation (SNSF)** was also among these institutions. However, as the aim of this paper is to list and summarize the foreign or international grant opportunities, we do not go into more details on the Swiss National Fund (SNSF) grants, which are well known to the Swiss expert community. It is nevertheless important to highlight that there are agreements and programs to fund cross-border research projects. Indeed, the national agencies also manage international programs that can be divided into three general categories:

- ✓ **Bilateral Cooperation** – normally based on a bilateral agreement between two countries. Within the framework of such agreements, common research projects are supported and funding is provided for several different types of activities. In Switzerland, the SNSF has a mandate from SERI to conduct calls for Joint Research Projects (JRPs) in collaboration with Argentina, Brazil, China, India, Japan, Russia, South Africa and South Korea. The JRPs will enable researchers from Switzerland to address specific research questions together with researchers from the above-mentioned partner countries.
- ✓ **Multilateral Cooperation** such as IRDIRC (see under)
- ✓ **Cooperation with the European Union** (EU), such as ERA-NET and EJP (see under)

The SNSF is of course the most relevant funding structure for Swiss experts. However, as the multidisciplinarity of rare diseases projects often requires transnational approaches, some grants allocated by other countries' national funding agencies are also available for foreign institutions.

Finally, **university research funding** is also partly financed by state funding. It is an important source of financing for health research. In 2017, Switzerland for example spent 0.76 percent of its GDP on university research funding[3]. Universities also offer advice and support to the researchers regarding the acquisition of third-party funds for research projects. Many of them have tools and databases to help searching for funding.

Here is the list of the most important agencies of some of our neighbouring countries and international partners:

1. ***France:*** The most important public funding structures are ***Institut national de la santé et de la recherche médicale (Inserm), Agence nationale de la recherche France (ANR) and Centre***

[1] *Viergever, R.F., Hendriks, T.C.C. The 10 largest public and philanthropic funders of health research in the world: what they fund and how they distribute their funds*, Health Res Policy Sys 14, 12 (2016). https://doi.org/10.1186/s12961-015-0074-z

[2] E-Rare 2, Work package 2 under the lead of ISS Italy (Domenica Taruscio), *Rare Disease Research Funding, Cross-sectional Analysis*, p. 16.

[3] OECD Science, Technology and R&D Statistics, Research and Development Statistics (Gross domestic expenditure on R-D by sector of performance and source of funds), 2017, accessible sur: https://stats.oecd.org/.

National de la Recherche Scientifique (CNRS)

Inserm is a french public research organization entirely dedicated to human health. Its objective is to promote the health of all by advancing knowledge about life and disease, treatment innovation, and public health research. Inserm has more than 6'000 scientific collaborations with foreign partners and more than 50% of their scientific publications are co-authored by foreign partners.

French National Research Agency (ANR) develops partnerships with funding agencies in different countries to facilitate the co-funding of transnational research projects and strengthen cooperation between French teams and the best European and international teams. The Agency also establishes bilateral non-thematic "Lead Agency"-type agreements with counterparts in European countries (Germany, Austria, Switzerland, Luxembourg), where one agency takes charge of project submissions and evaluations.

The National Centre for Scientific Research (CNRS) is an interdisciplinary public research organization under the administrative supervision of the French Ministry of Higher Education and Research. The CNRS has set up structured cooperation mechanisms to strengthen its presence worldwide. These include for example 37 international joint units.

2. ***Germany:*** The two main public funding structures are ***Deutsche Bundesministerium für Bildung und Forschung (BMBF) and the German Research Foundation (DFG)***: At national level, the BMBF has been promoting the formation of networks that bring together research and treatment capacities since 2003. Currently, ten research collaborations are being promoted as part of the funding program for application-oriented basic research and collaborative projects in the field of rare diseases. In 2018, the BMBF made available EUR 21 million for the next four years to study rare diseases. Research for Rare www.research4rare.de is a German network on Rare diseases constituted under the BMBF. They organize international networking events such as the Symposium „The Translational Science of Rare Diseases – From Rare to Care III".

   The DFG offers different opportunities to enable researchers to participate in international cooperation. Proposals with international participation can be submitted on any topic, as long as they satisfy the funding principles. Specific funding opportunities are also offered in partnership with foreign partner organizations. The DFG also provides information in the form of various databases to help researchers in other countries find out about the research landscape in Germany.

3. ***United Kingdom: UK Medical Research Council and National Institute for Health Research (NIHR):*** The NIHR is UK's largest funder of health and care research. They work in partnership with the NHS, universities, local government, other research funders, patients and the public. They are primarily funded by the Department of Health and Social Care.

   The Medical Research Council (MRC) is responsible for coordinating and funding medical research in the United Kingdom. The MRC works in partnership across UK Research and Innovation and with the National Institute for Health Research (NIHR) and devolved administrations, the NHS, charities and industry. Their molecular and cellular medicine portfolio focuses on basic biological mechanisms or technologies relevant to human health and disease, including understanding the aetiology of disease and developing treatments. Most of the MRC grants are designated to UK institutes and organisation but MRC participates in many international collaborations and programs. Furthermore, the UK's Fund for International Collaboration (FIC) aims to enhance excellence in research and innovation through global engagement.

4. ***USA: National Institute of Health (NIH)*** is the world's biggest funder of health research. It is part of the United States Department of Health & Human Services. NIH is the primary U.S. Federal agency that conducts and supports medical research. To realize its mission of extending healthy life and reducing the burdens of illness and disability, NIH funds grants, cooperative agreements, and contracts that support the advancement of fundamental knowledge about the nature and behaviour of living systems. The 27 Institutes and Centers (ICs) of NIH provide leadership and financial support to researchers both inside and outside the United States. Approximately 80% of NIH funding goes to support research grants, including grants to foreign organizations. Many of the ICs have international programs/collaborations. With few exceptions, the applications for research grant support from foreign organizations are treated as if they were applications from domestic organizations. Information for foreign grants can be found here.

   For other funding opportunities in the US, see for example the list published by American Association of Colleges of Pharmacy accessible here.

5. ***Canada: Canadian Institutes of Health Research*** (***CIHR-IRSC Canada***) is the major federal

agency responsible for funding health and medical research in Canada. Another important fund that deserves to be highlighted is *Fonds de recherche du Québec*. To date, CIHR has supported an increasing number of research grants and training awards with an international focus through its Investigator-Driven Research and Priority-Driven Research Funding programs. CIHR has over 60 international agreements (however, no agreement with CH) and Canadian researchers are currently working with researchers in 75 countries.

6. ***Australia*: Australian National Health and Medical Research Council (NHMRC)** is an independent statutory agency within the portfolio of the Australian Government Minister for Health and Ageing, operating since 2006 under the National Health and Medical Research Council Act 1992. It is the Australian leading expert body in health and medical research. NHMRC assists Australian researchers to participate in collaborative research projects with international researchers through both bilateral and multilateral arrangements.

B) INTERNATIONAL AND EU FUNDING STRUCTURES

A list of different funding opportunities in the area of rare diseases at the EU level can be found under this link: https://ec.europa.eu/info/research-and-innovation/research-area/health/rare-diseases_en

1) **International Rare Disease Research Consortium (IRDiRC)** aims to accelerate and coordinate rare diseases research efforts around the world involving more than 50 organizations investing in rare diseases research including the European Commission. It was founded in 2011 by the European Commission and the US National Institute Health (NIH). IRDiRC has the ambitious long-term vision to enable all people living with a rare disease to receive an accurate diagnosis, care, and available therapy within one year of coming to medical attention.

   In April 2019, IRDiRC's Interdisciplinary Scientific Committee (ISC) established a Task Force on Clinical Research Networks for Rare Diseases aiming to map and analyze the existing ecosystem of national/supranational clinical research networks, and develop policy recommendations on guiding principles for an international framework of collaboration of these networks.

2) **European Framework Programs: Horizon 2020 (2014-2020) and Horizon Europe (2021 -2027)**

   Note on the Swiss participation: Switzerland has a bilateral agreement with the EU in this field and retrieves the full association to the entire Horizon 2020 programme from 01 January 2017[4]. Switzerland and the EU share long-standing and successful cooperation ties in the area of research and innovation. Swiss participation in the EU research framework programmes is part of the first series of bilateral agreements between Switzerland and the EU that came into effect in 2002. It does not involve market access issues and is therefore not part of the current discussions on an institutional framework agreement. Switzerland thus expects to be able to participate in Horizon Europe and is committed to this objective. SERI publishes regular updates on Horizon Europe (see Further information).

   The European Commission has made major investments in research and innovation in rare diseases for more than two decades throughout the EU Framework Programmes for Research and Innovation. Altogether more than € 1.4 billion has been committed in research and innovation through the Seventh Framework Programme (FP7) and Horizon 2020 in more than 200 projects related to rare diseases. EU-funded research projects results in the area of rare diseases can be found on the Commission's primary portal website the Cordis and in this factsheet established by the EU Commission.

   Horizon Europe (HE) is the successor to Horizon 2020 – the new framework programme of the European Union (EU) on research and innovation (R&I) for 2021-2027. This ambitious programme has a €100 billion budget and is the EU's leading initiative to support R&I from concept to market, complementing national and regional funding. HE has been designed to support partnerships between EU countries, the private sector, foundations and other stakeholders, and aims to deliver on global challenges and industrial modernisation through concerted R&I efforts. For the Health Cluster, a total of 6 key areas of have been identified, namely: health throughout the life course; environmental and social health determinants; NCDs and rare diseases; infectious diseases; healthcare systems, and tools, technologies and digital solutions for health and care.

   European Research Council (ERC) complements other funding activities in Europe such as those

[4] For more information, see https://www.sbfi.admin.ch/sbfi/en/home/topics/swiss-international-cooperation-in-research-and-innovation/european-union-framework-programmes-for-research/horizon-2020-_-the-european-unions-framework-programme-for-resea/swiss-transitional-measures-for-horizon-2020.html

of the national research funding agencies. The ERC projects are also part of the 200 Horizon 2020 projects on rare diseases listed in the beyond mentioned factsheet of the European Commission.

One of the most relevant projects funded by the Health Program of Horizon 2020 in the field of rare diseases is the European Joint Programme on Rare Diseases (EJP RD), launched in 2019

European Joint Programme on Rare diseases (EJP RD) is the fourth generation of the ERA-Net E-Rare. Diseases aims at improving the cooperation and coordination of research initiatives in EU member states and associated states. Since 2006 the ERA-Net projects for Rare Diseases (E-Rare) have provided funding over to €100 million to more than 100 collaborative projects on rare diseases research through joint calls for proposals. Its international dimension was directly translated into close collaboration with IRDiRC and other relevant European and international initiatives.

EJP RD aims at establishing a research and innovation pipeline ensuring rapid translation of research results into clinical applications and uptake in healthcare. It also aims to coordinate research efforts in the area of rare diseases among European and non-European countries. EJP RD involves research funders, universities, research organisations, research infrastructures, hospitals and patient organisations from 35 countries including 27 EU Member States, seven Associated Countries, incl. Switzerland and Canada. The EJP RD will foster annual Joint Transnational Calls (JTC) for collaborative research projects resulting in funding encompassing various research fields of rare diseases in continuation of previous E-Rare calls. Information on the current calls for proposals can be found here.

Innovative Medicines Initiatives (IMI) is a partnership between the EU and the European pharmaceutical industry. As such, it is funded half by the EU's research and innovation programme and half by large companies from the pharmaceutical sector. The goal of the IMI is to improve health by speeding up the development of, and patient access to, the next generation of medicines, particularly in areas where there is an unmet medical or social need. For 2014-2020 IMI's strategic focus particularly included research on rare diseases. It does this by facilitating collaboration between the key players involved in healthcare research, including universities, pharmaceutical companies, patient organizations and medicines regulators. One example of the projects financed by IMI 2 is the c4c (conect4children), a large collaborative European network that aims to facilitate the development of new drugs and other therapies for the entire paediatric population. The network gathers the academic and the private sectors, including 33 academic and 10 industry partners from 20 European countries, and more than 50 third parties and around 500 affiliated partners. The project has received funding from the Innovative Medicines Initiative 2 Joint Undertaking. The Joint Undertaking receives support from the European Union's Horizon 2020 research and innovation programme and EFPIA.

Joint Programming Initiatives (JPIs) are Horizon 2020 instruments developed in a structured and strategic process where EU countries agree on a voluntary basis on common visions and Strategic Research Agendas (SRA). The aim of the joint programming process is to pool national research efforts in order to make better use of Europe's research and development resources and tackle common European and major societal challenges more effectively. JPIs can also be relevant for rare diseases field. For example the JP on 'Alzheimer and neurodegenerative diseases' (JPND) also covers rare neurodegenerative diseases.

4) Rare Disease-Action **(RD-Action)** is a Joint Action funded by the third EU Health Programme (2014-2020). It unites 34 beneficiaries and 30 collaborating partners from 40 countries. RD-Action's main goal is to create an integrated European approach to the challenges faced by the rare diseases community and to ensure the development and sustainability of Orphanet databases (the biggest global repository of information on rare diseases). In addition to EU Member States, other European countries, including Switzerland, as well as non-European countries such as Canada and Australia, participate in the programme.

5) Other related European initiatives in the field of research:

- ✓ **EATRIS: European Infrastructure for Translational Medicine** aims to provide infrastructure to allow a faster and more efficient transfer of research discoveries into new products to prevent, diagnose or treat diseases.
- ✓ **ELIXIR**: The European Life Sciences Infrastructure for Biological Information is an initiative that will allow life science laboratories across Europe to share and store their research data as part of an organised network.
- ✓ **Europhenome Mouse Phenotyping** project provides access to raw and annotated mouse phenotyping data generated from primary pipelines such as EMPReSSlim and secondary procedures from specialist centres. Mutants of interest can be identified by searching the gene

or the predicted phenotype.

- ✓ **European Platform on Rare Disease Registration** (EU RD Platform) is open to all RD registries in order to act as a knowledge of generation centre benefiting healthcare providers including European Reference Networks, researchers, patients and policy-makers in the common effort to improve diagnosis and treatment for patients living with a rare disease.
- ✓ **ERAWATCH** is the European Commission's information platform on European, national and regional research systems and policies. Its main objectives are to support policy-making in the research field in Europe and to contribute to the realisation of the European Research Area (ERA). The service currently covers 61 countries: 28 EU Member States, countries associated with the European Community's Research Framework Programme and, for comparative purposes, main trading partners of the EU.
- ✓ **Solve RD** project (solving the unsolved rare diseases) has received funding from the European Union's Horizon 2020 research and innovation programme. The Solve-RD consortium consists of 21 European academic institutions and 1 academic partner from the United States. Clinicians from a Solve-RD beneficiary or associated partner institution can submit an application for a newly discovered disease gene, which they would like to be functionally validated. The European Rare Disease Models & Mechanisms Network (RDMM-Europe), mentioned above (part I) has been established by Solve-RD.
- ✓ **European clinical research infrastructure network (ECRIN)** is a public, non-profit organisation that links scientific partners and networks across Europe to facilitate multinational clinical research. They provide sponsors and investigators with advice, management services and tools to overcome hurdles to multinational trials and enhance collaboration.
- ✓ **European Network for the advancement of Clinical Gene Transfer & Therapy (CliniGene-NoE):** Its aim is to mobilize efficiently all interested parties, mostly involving academic research and production centres together with companies, patients' groups and regulatory bodies. Its main goal is to integrate multidisciplinary research in order to decipher the key elements, which can lead to improved safety and clinical efficacy of gene transfer / therapy medicinal products, i.e. for clinical applications.
- ✓ **Human Phenotype Ontology (HPO)**: An ontology is a computational representation of a domain of knowledge-based upon a controlled, standardized vocabulary for describing entities and the semantic relationships between them. The Human Phenotype Ontology (HPO) aims at providing a standardized vocabulary of phenotypic abnormalities encountered in human disease.
- ✓ **European Cooperative in Science and Technology (COST)** is a research initiative that makes it possible for the various national facilities, institutes, universities and private industry to work jointly on a wide range of Research and Development (R&D) activities. COST invites researchers throughout Europe to submit proposals for research networks and use this opportunity to exchange knowledge and to embark on new European perspectives. The support will cover the costs of networking activities such as meetings (e.g. travel, subsistence, local organiser support), conferences, workshops, short-term scientific exchanges, training schools, publications and dissemination activities. COST does not fund the research itself.

6) Other related international and multilateral initiatives and research consortiums

Although the following international initiatives are not directly linked to rare diseases, they can still be relevant for the research in the field of rare diseases:

- ✓ Global Alliance for Genomics & Health (GA4GH) is a policy-framing and technical standards-setting organization, seeking to enable responsible, voluntary, and secure genomic data sharing within a human rights framework. The GA4GH was founded in 2013 as an international consortium bringing together 500+ leading organizations working in healthcare, research, patient advocacy, life science, and information technology. The GA4GH is maintained by three host institutions (Wellcome Sanger Institute, Broad Institute, and Ontario Institute for Cancer Research) and funded by the Canadian International Data Sharing Initiative and the US National Institutes of Health.
- ✓ Human Frontier Science Program (HFSP) promotes international collaboration in basic research focused on the elucidation of the sophisticated and complex mechanisms of living organisms. The HFSP receives financial support from the governments or research councils of 13 countries including Switzerland.
- ✓ International Agency for Research on Cancer (IARC) is the specialized cancer agency of the World Health Organization. The objective of the IARC is to promote international collaboration in cancer research. ARC plays an important role in catalysing international collaborations with

Joint publications, coordination and collaboration in research consortiums.

- ✓ International Cancer Genomics Consortium (ICGC) is a research consortium established in 2007, which aims to define the genomes of 25,000 primary untreated cancers and to provide the international community with comprehensive genomic data for these cancer types. The ICGC is funded by its participating member entities from 15 countries around the world.
- ✓ International Human Epigenome Consortium (IHEC) is a global consortium with the primary goal of providing free access to high-resolution reference human epigenome maps to the research community. IHEC's operations are funded by its 8 full members, and staffed largely on a volunteer basis by scientists and other experts from participating funding agencies. IHEC facilitates communication among its members and offers a forum for coordination, with the objective of avoiding redundant research efforts and implementing high data quality standards.
- ✓ International Human Microbiome Consortium (IHMC) is an initiative for international researcher to work under a common set of principles and policies to study and understand the role of the human microbiome in the maintenance of health and causation of disease. The IHMC is financed by various research funding agencies and the US National Institutes of Health. It is open for membership from any researchers who agree to the consortium's principles such as the sharing of data, common quality standards and a common publication policy.
- ✓ Networks of Centres of Excellence in Neurodegeneration (COEN) is an initiative based on a joint programme initially agreed in 2010 between the Canadian Institutes of Health Research, the Deutsche Zentrum für Neurodegenerative Erkrankungen and the UK Medical Research Council. The initiative was subsequently joined by research institutes from Belgium, Ireland, Italy, Spain and Slovakia. The overall aim of the initiative is to build collaborative research activity in neurodegeneration research across borders, focusing on the critical mass and excellence.

7) Cross-border projects under different Interreg Programs (FR-CH, CH-ITA, CH-D, CH-AUT)

Interreg programs are part of the EU's Regional Cohesion Policy. Switzerland has been participating in Interreg programs with its Neighboring Countries (I, D, AUT or F) since their beginning in the early nineties. Today the main purpose of these programs is the cross-border economic development. Interreg offers possibilities to develop cross boarder or transnational projects in numerous fields including health. The EU funds and the participating neighboring country finance one part and cantons, Swiss confederation and other private or public partners finance the Swiss part.

The fifth programming period (Interreg V) started in 2014 and ended in 2020. The preparation of the new 2021-2027 phase (Interreg VI) is currently underway at the European Commission as well as under the various regional programs (*state of the play: Feb. 2021*). The Interreg V program had three components, in which Switzerland also participates: 1) Interreg A: cross-border programs between regions sharing a common border. Switzerland is involved at cantonal level in 4 different Interreg A programs: Upper Rhine (cantons AG, BL, BS, JU, SO), Rhineland Alps-Lake Constance-Haut-Rhin (cantons AG, AI, AR , GL, GR, SG, SH, TG, ZH), Italy-Switzerland (cantons GR, TI, VS) and France-Switzerland (cantons BE, FR, GE, JU, NE, VD, VS). 2) Interreg B are transnational programs and 3) Interreg C interregional programs covering both broader regions or involving several countries. The latter two are less relevant for the health field.

The list of different financing instruments and aids can be found here: https://regiosuisse.ch/fr/aides-financieres-developpement-regional The data basis of existing and passed projects is available under the following link https://regiosuisse.ch/fr/projects-nrp . Under the Interreg V, many projects in the field of health have already been financed. They cover for example projects aiming at discovering a new drug; developing new health technologies and tools for diagnosis. These projects can also cover rare diseases.

C) FOUNDATIONS & PHILANTHROPIC FUNDERS, PRIVATE RESEARCH INSTITUTES, PHARMACEUTICAL COMPANIES GRANTS & FELLOWSHIPS

1) **Pharmaceutical Companies** are major funding bodies for the research in the field of rare diseases. Almost all pharmaceutical companies have their **Grant programs and awards**.

   Some companies also have different Fellowship programs. Fellowships serve as 1- or 2-year postdoctoral training programs to help pharmacy graduates develop into industry professionals. In many programs, industry fellowships are joint ventures between universities and pharmaceutical companies.

2) Biggest international Philanthropic funders of biomedical research

Preliminary remark: We only include in this list foundations whose primary goals cover rare diseases or whose main focus lies within biomedicine and biotechnology research work. The biggest philanthropic foundations in the health field, such as Bill & Melinda Gates Foundation (BMGF), whose primary goals are to enhance healthcare globally, are not necessarily relevant for rare disease research.

- ✓ **Wellcome Trust** is a research charity foundation based in London. The Trust funds biomedical research (including in the field of rare diseases) and supports the public understanding of science.
- ✓ **Howard Hughes Medical Institute** (HHMI) is one of the world's largest philanthropies aiming at advancing of knowledge within the basic sciences. The Institute carries out its mission across the United States but their international programs extend the impact of HHMI's investment to 17 countries around the world.
- ✓ **Novo Nordisk Foundation** is one of the biggest international foundation focusing on medical treatment and research. The Foundation distributes more than 300 million US dollars each year to research within the fields of Life- and Bioscience.
- ✓ **Broad Institute** is based in Boston/USA but their activities extend beyond the Boston area, including more than 100 projects across more than 40 countries. Broad researchers study several rare inherited diseases, including muscle disorders, mitochondrial disorders, and kidney disease**.** Resources used in Broad's studies of rare disease include data from the 1000 Genomes Project and the Exome Aggregation Consortium (ExAC). The Broad's Clinical Research Sequencing Platform (CRSP) also performs genetic sequencing of patients with rare disorders, producing data for research or clinical use. The Broad Center for Mendelian Genomics focuses on large-scale sequencing of patients with rare diseases, in collaboration with many clinical investigators.
- ✓ **LifeArc** is a UK registered and self-funding Philanthropic Fund, which supports translational rare disease research projects. Focus is on developing an intervention (therapeutic, device or diagnostic) that will address a significant, unaddressed need for rare disease patients and on research which has a credible translational and development path to reaching patients.

In Switzerland, there are also foundations that finance research activities in the field of rare diseases or in connected health areas. The list can be found in the Swiss electronic directory of foundations. For example, EspeRare, a nonprofit organization established in 2013, aims at uncovering the potential of existing therapies to address severe therapeutic unmet needs in rare diseases. the Swiss Blackswan Foundation is recognized by EURORDIS as the voice of the rare disease researchers within its action of advocacy towards the UN and WHO. The Foundation supports research nationally and internationally. For this purpose, they also organize every second year the RE(ACT) Congress, a unique human platform for networking and knowledge sharing supported by EJP RD. Other Foundations with more wide-ranging goals can also serve the purpose of rare disease research. For example, Botnar Foundation invests in emerging solutions (Artificial intelligence and new technologies) to build a better future for children and young people globally. The Foundation provides a range of funding opportunities to enable research and innovation within their focus.

3) Other foundations and research organisations

- ✓ **ESF European Science Foundation** counts 78 Member Organisations (MOs), including research funding organisations, research performing organisations, academies and learned societies, in 30 countries. It is an independent, non-governmental organisation dedicated to pan-European scientific networking and collaboration. Each year, the ESF announces a series of calls for proposals for collaborative research projects and networking activities with a European dimension. The calls span all fields of science through different funding instruments, covering all types of scientific activities, from basic research and frontier science to networking and dissemination**.**
- ✓ **Science Europe** is an association of European research funding organisations and research performing organisations, based in Brussels. Science Europe promotes the collective interests of the research funding and research performing organisations of Europe. Science Europe's 37 member organisations from 28 European countries are among the most important public research organisations funding and performing scientific research in Europe.
- ✓ **European Molecular Biology Organisation's (EMBO)** mission is to enable the best science by supporting talented researchers, stimulating scientific exchange and advancing policies for a world-class European research environment. EMBO membership consists of over 1,800 of the world's leading life scientists. EMBO offers awards and financial support for scientists at all stages of their careers.
- ✓ **Task Force on Rare Neurological Diseases (RDN) of the** European Academy of Neurology **(EAN):** The list of the RND encloses more than 5,000 disorders.
- ✓ **European Organisation for Research and Treatment of Cancer (EORTC)** is an independent,

non-profit cancer research organisation whose mission is to coordinate and conduct international translational and clinical research activities across 35 countries to improve the standard of cancer treatment for patients.

- ✓ **PhRMA Foundation Research Starter Grants** The PhRMA works to improve public health by proactively investing in innovative research, education and value-driven health care.
- ✓ **The European Society of Gene and Cell Therapy (ESGCT)** promotes basic and clinical research in gene therapy, cell therapy, and genetic vaccines by facilitating education, the exchange of information and technology and by serving as a professional adviser to stakeholder communities and regulatory bodies in Europe.
- ✓ **Findacure** is s a UK charity that is building the rare disease community to drive research and develop treatments.
- ✓ **Kindness for Kids** is a German foundation that was founded with the goal to improve the situation of children with rare diseases through both social projects and funding for research. In 2014, Kindness for Kids established a new research funding program, focusing on basic and health services research.
- ✓ **The Care-for-Rare Alliance** and the Care-for-Rare Foundation based in Germany supports international research projects. It is expanding the worldwide network of academic centers of excellence for children with rare diseases. The Foundation offers prestigious awards to support young clinicians and scientists to initiate a promising new research project on rare diseases.

4) **International databases** useful for the search of funding opportunities:

- ✓ **SPIN** (the Sponsored Programs Information Network) is run by InfoEd International and is one of the most widely used funding opportunity database in the world. An institutional subscription is required for access.
- ✓ **ResearchResearch** - Based in London, ResearchResearch provides an international option for people seeking research-funding programs. A paid subscription is required for access.

D) MAIN PATIENT ADVOCACY GROUPS WITH RESEARCH GRANTS AND FUND RAISING

Finally, even though this paper does not cover the patient organizations and networks, we mention three relevant organizations who also play an important role in fund raising and provide research grants:

1) **Rare Disease International (RDI)** is the global alliance of people living with a rare disease. RDI brings together national and regional rare disease patient organizations from around the world as well as international rare disease-specific federations. The RDI Fellowship Programme empowers patient advocates by offering a platform for networking opportunities, access to information and sharing experiences at international level. The Fellowship Programme is primarily focused on supporting patient engagement in international fora where RDI is active or there is strategic interest on the part of RDI to become active. The programme can also cover capacity building opportunities.

2) **Rare Diseases Europe (EURORDIS)** is a non-profit alliance of 884 rare disease patient organizations from 72 countries. They bring together patients, families and patient groups, as well as other stakeholders. EURORDIS aims at mobilizing the rare disease community, strengthening the patient voice and shaping research, policies and patient services.

3) **National Organisation for Rare Disorders (NORD)** is an American patient advocacy organization dedicated to individuals with rare diseases and the organizations that serve them. They offer database, programs and platforms where rare disease patients and professionals can inform, fundraise, communicate and advocate. NORD's Research Grant Program provides seed grants to academic scientists for translational or clinical studies related to development of potential new diagnostics or treatments for rare disease. NORD has also created a Natural Histories Patient Registry Platform that allows patients and organizations to inform and shape medical research and translational science for rare diseases by launching high-quality, customized registries to collect the data needed to define the natural progression of their disease – ultimately advancing product development.