

Part I

The Netherlands





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Part I

Key learnings Executive summary Netherlands





The Netherlands

«The Dutch R&D model is characterized by a strong innovation system, unique mix of businesses working alongside world-class knowledge institutes from agriculture to transportation, with a highly skilled workforce and attractive R&D incentives»



The Netherlands

	Pain points	Success stories	Opportunities
Education	 Stretch in development of talents vs current and future demand Need for more entrepreneurship skills Digitalization 	 Strong partnerships with Industry at Educa tional level (collaborative campus schemes) Collaborative model for the Dutch Centres for Entrepreneurship 	 Collaborative models National Strategy for innovation and talent Attractiveness of the Dutch university and educat ion system
Innovation	 Fragmented High competition between hubs and regions within the country Does not house the HQ of large Pharma or Biotech companies 	 Centre for BioScience and Diagnostics – Training facility for GMP Brightlands Campus 	 Strong <u>digital infrastructure</u>, <u>14 universities</u> <u>R&D incentives</u>
Business	 Regulatory constraints Complex and fragment funding landscape Limited presence of large Pharma or Biotech 	 Brabant biopharmaceutical research campus <u>Pivot Park</u> Netherlands Center for the Clinical advancement of Stem Cell and Gene Therapies (NECSTGEN) 	 Cross-sectorial collaboration (i.e AgroFood) Transport hub Digital hub One of Europe's largest start-up ecosystems High level of public-private partnerships









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Contributions



Part II

National Context Specificities Netherlands





National Context Specificities

The Netherlands ranks third in the world for overall logistics performance,. Amsterdam

Schiphol airport connects 327 international destinations directly (2018). The direct connections of Amsterdam Schiphol offer a clear logistical advantage to therapy developers when thinking about complex supply chains, patient material and therapy shipment

IT infrastructure

Microsoft, Cisco, Oracle, Intel, IBM, Verizon, and Google, all tap into the unparalleled IT infrastructure backed up by the Amsterdam Internet Exchange (AMS-IX), the world's largest data traffic hub. Furthermore, the Netherlands is also a leader in the digitalization of healthcare with around 87% of patient-related data carried in digital records.

Regulatory science & innovation

The relocation of the European Medicines Agency to Amsterdam bolsters the work of the MEB and provides a significant opportunity for the Netherlands to further strengthen its position as a frontrunner in regulatory innovation in Europe.

A prime example is Escher. Escher's purpose is to promote research and international debate in the field of policy and regulations relating to development, market authorization, reimbursement, and use of medicines and medical technology in order to create an efficient and effective regulatory system.





EUROPEAN MEDICINES AGENCY







Part II.A

Tackling the talent gap and the talent crunch in biomanufacturing in Europe < ___





The Netherlands have strong academics forces



worldwide for medical technology patent applications



worldwide for biotechnology patent applications





BioTech Delft organises biotechnology education at postgraduate level. BioTech Delft is coordinated from the <u>department of Biotechnology</u> of <u>Delft University of</u> <u>Technology</u>. At the department we perform state-of-theart research for the design of bioprocesses and all underlying aspects.

Since its foundation in 1987, BioTech Delft has very successfully organised various types of short in-depth courses. We closely cooperate with leading experts from industry and academia.







The Netherlands and talent development



European Union

Per one million inhabitants:





Success story - Leiden Bio Science Park

LEIDEN BIO SCIENCE PARK

The leading life sciences hotspot in the **Netherlands**

Leiden Bio Science Park ranks among the top five m successful science parks in Europe. It is fully dedicated to biomedical life sciences and offers opportunities for both established companies and start-ups to flourish. https://leidenbiosciencepark.nl/

Leiden Bio Science Park counts





The entire range of studies in academic education (WO), higher professional education (HBO) and intermediate vocational education (MBO) is offered at LBSP.

Leiden Bio Science Park conducts research mathematics, computer science, chemistry, biology and medicine

Leiden Academic Centre for Drug Research (LACDR) runs a special PhD programme focused specifically on drug development which strongly encourages entrepreneurship in students.

Leiden Academic Centre for Drug Research



American pharmaceutical company Bristol Myers Squibb will be building a new (CAR-T) cell therapy facility in the Oegstgeester part of the Leiden Bio Science Park. The company will manufacture and develop CAR T-cell therapy for patients with blood cancer (leukaemia), for example.

-lealth

Talent and Future of Skills: <u>Roadmap to human capital strategy</u>

The new mission-driven innovation policy has set new outlines for the Roadmap Human Capital top sectors 2020-2023. In the Roadmap, all top sectors bundle their capacities and share knowledge to invest in human capital as driving force to reach societal and economic goals.

In the Knowledge and Innovation Agenda 2020-2023 of the social challenge Health & Care, several deliverables for human capital are included, such as four to six learning communities and a transition agenda for the education for health and care professions in the Netherlands.

For the coming years the focus will be on three coherent programs : Innovate, Work and Learn

* Transition and intersections within the top sectors

Transitions in healthcare are at the intersection of life sciences & health, digitization and logistics.

* Cooperation and partnerships

Learning communities, Fieldlabs and Skillslabs to support the SER's Lifelong Development Action Agenda. Technology Pact and Katapult, innovations at a regional level more profitable in education and companies. Open innovation connects corporate R&D to Academic institutes

 Platform Talent for Technology (PTvT) and Technology Pact Concrete activities to combat the shortage of science technicians. Connection with the top sectors

The call: "Human Capital: learning communities as an innovation accelerator"

The focus of this call is on existing, starting or developing learning communities. A total of € 2,628,467 is available for this call. The Top Sector Life Sciences & Health is one of the funding partners

Consortia consist of researchers at Dutch universities, universities of applied sciences and other research institutes in collaboration with public and private partners from professional practice.

For each proposal, **between € 750,000 and € 1,000,000 in funding can be requested.** 15% of the total project costs must be pledged in the form of co-funding. A project may have a max duration of six years (72 months).

The deadline for submitting proposals is Tuesday 15 June 2021 at 2:00 PM CE(S)T







Part II.B

Research to









Key aspects

- Unique mix of businesses working alongside world-class knowledge institutes
- Innovation leader in Europe, ranking fourth on the 2020 European Innovation Scoreboard of the EU Commission.
- strong <u>digital infrastructure</u>, <u>14 universities</u> and openness to multidisciplinary and new ways of thinking
- The Dutch government offers <u>R&D incentives</u> for companies pushing boundaries in the Netherlands.
- 7% tax rate for income related to patents and associated development.



The power of public-private partnerships

Pragmatic solutions Dutch Public-Private Partnerships (PPPs) receive worldwide acclaim, especially in the areas of oncology, medical technology, bio-banks and vaccines. PPPs such as the Netherlands Genomics Initiative, CTMM and TI Pharma (both merged into Lygature) have set international standards. The entire healthcare-chain is typified by a strong inter-disciplinary approach that leads to pragmatic, holistic solutions - from bench to patient

l**y**gature

Lygature is a not-for-profit organization based in the Netherlands. It drives the development of new medical solutions for patients by managing publicprivate partnerships involving academia, industry and society. Every day, Lygature brings together people in many different disciplines and organizations – to pioneer solutions in medical technology and pharmacotherapy, and to serve patients worldwide.

"To develop vaccines against pathogens of global concern, such as Ebola, HIV and AMR bacteria, partnerships are essential. In the Netherlands, Janssen Vaccines can collaborate with many high-ranking academic institutes, and it is a breeding ground for biotech start-ups. This creates a climate of cooperation that allows us to stay a frontrunner in our field."



Johan van Hoof, Global Head of Vaccines R&D at Janssen



The Netherlands has several measures in place that promote research & development. $\overleftarrow{8}$

These include general corporate and specific R&D tax incentives. These pro-innovation R&D tax measures not only cut R&D costs but also lower a company's taxable base.

- The WBSO tax credit is an example of a scheme for businesses involved in developing technically new products and production processes as well as those performing scientific research in biotechnology, physics, chemistry, production technology and IT technology. Clinical trials are also included in this scheme. The WBSO provides a payroll tax deduction as well as compensation for other costs for companies involved in R&D.
- Companies may be entitled to as much as a 32% reduction on the first 350,000 euros in R&D wage costs and other R&D-related expenses, and 14% for costs over 350,000 euros. Public knowledge institutes are excluded from the scheme.





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Under the Innovation Box initiative, companies can benefit

- from an effective tax rate of only 7% for R&D income from patented and unpatented intangible assets.
- This includes technological innovations created by the Dutch taxpayer and for which an R&D tax credit was received.
- The normal corporate income tax rate is 20% to 25%.
- Companies are not required to apply for the Innovation Box and the level of income allocated is restricted.
- This means that as more R&D activities are outsourced, fewer profits can be allocated to the intangible assets that result from these activities.

There is a flat-rate regulation

- for SMEs, which can decide each year to apply 25% of their profits to the Innovation Box with a cap of 25,000 euros.
- The corporate income taxpayer claims the lower 7% rate on their return.
- The lower rate is, in fact, an exemption of 72% of the profits that can be allocated to the Innovation Box, giving an effective rate of approximately 7%.
- The effective rate applies to profits exceeding any development costs and losses made.
- Such losses and expenses are deductible at the normal tax rate of 25%.



- Use Case : Artificial Intelligence Lab for Biosciences (the AI4B.io Lab)

Al for Biosciences Lab (AI4B.io Lab) is a collaboration between Delft University of Technology and DSM. The lab focuses on improving production technologies and developing bio-based products using AI.

AI4B.io Lab is the first of its kind in Europe to apply artificial intelligence to full-scale biomanufacturing, from microbial strain development to process optimization and scheduling. AI4B.io Lab is aimed at long-term innovation in the domain of AI for developing biobased products and optimizing biobased production technologies.

It targets to develop a deep understanding of how novel AI technology (methods, techniques, theories, and algorithms) can strengthen the effectiveness and efficiency of relevant research and/or business processes in the biotech industry.

Main tracks of Research:

Developing an AI-based framework/advisory tool for optimal batch scheduling to maximize plant output of an enzyme production line, and balance product performance and quality against operational costs.

Digital twin for larg-scale fermentation

Evaluate how AI methods can be applied to develop an accurate real-time simulation of fermentation performance indicators in response to dynamic process inputs for industrial scale fed-batch operated fermentation units of 50-500 m3.

Digital twin of lab automation processes and self-learning platforms

Developing autonomous systems that evaluate and develop 'self-learning' experimental design algorithms, combine data-driven approaches with mechanistic modeling and other things.

Machine learning for genomephenotype engineering

Evaluating and implementing so-called 'representation learning' methods on multiomics data from strain development projects.

Machine learning for iterative metabolic engineering

DSM

To determine how AI/ML methods can support efficient exploration of a large solution space for (iterative) strain improvement.











One ecosystem



Four areas of expertise

Brightlands Chemelot Campus Smart materials and sustainable production of chemicals IO2 companies / 2 771 jobs / 1173 students

Brightlands Maastricht Health Campus

egenerative medicine, precision medicine, innovative diagnostics 20 companies / 9.652 iobs / 7.397 students

Brightlands Campus Greenport Venlo

Safe and healthy nutrition, future farming, and bio-circular economy



Brightlands Smart Services Campus Data science and smart services 80 companies / 900 iobs / 450 students

companies / 660 jobs / 1,200 students

nnovation

story

www.brightlands.com

From generic to innovative medicines **Basic** Pharma

Brightlands > Chemelot Campus > News & Events > Blogs & Stories > From generic to innovative medicines

Basic Pharma set up operations over ten years ago at the Van Iterson building, a former DSM property on the outskirts of the Brightlands Chemelot Campus. Considered too large at the time for the 20 employees working there, these days, serious plans are being made for new construction. The new facility will have room for what is now over 100 employees, and is better suited to meet current needs. "We've outgrown our space again."

Limburg region

High participation of larger companies such as Lonza and DSM, in the development and cross-research initative between the different campuses

The research institutes at Brightlands Chemelot Campus - AMIBM, Brightlands Materials Center, Chemelot InSciTe, CHILL and Brightsite - are application-driven.

Fundamental research is promoted by Maastricht University. Within the biomedical ecosystem, Brightlands Chemelot Campus works closely with the research centers at Brightlands Maastricht Health Campus and its fundamental research institutes Medace, Merlin and Carim.







@ Brightlands, June 2020







Opportunities - International health initiatives

56 MILLIONS FOR REGENERATIVE MEDICINE



The RegMed XB consortium, of which TU/e is a member, will receive €56 million from the Growth Fund to bring regenerative medicine to the market, consisting of an allocation of €23 million and a conditional allocation of €33 million.

This collaboration of research institutions, public authorities, provinces, health funds and industry in the Netherlands and Flanders develops therapies for chronic diseases, based on stem cells, mini-organs, tissues and smart (bio)materials



European Lead Factory **EFPIA** contribution European (>300.000 cpds) Compound Collection Public LIBRARY contribution DESIGNS (200.000 cpds by 2017 ♣ • uHTS / HCS Compound logistics European DRUG TARGETS AND PHENOTYPES Screening Hit triage and confirmation Centre

An example of a successful PPP is the European Lead Factory, whose mission is to deliver innovative drug discovery starting-points.

The European Lead Factory has founded the European Compound Library and the European Screening Centre - a unique industrystandard uHTS platform offering free access to up to 500,000 novel compounds.









Part II.C

Business







Provide and a set of the set of

The Netherlands have a diverse ecosystem of industries and research centers active in the Biomanufacturing and Advanced therapy field

- High number of Contract development and manufacturing organizations (CDMO)
- Products and services companies from the Agro-Food and Energy sector to design the bioprocesses and connect with the LifeScience sector
- Taks incentives

+33

billion

+29

billion

• Headquarters of several pan-European initiatives and agencies such as EMA, EATRIS

2900

420

• Turnover

Production

value

Key example of LifeSciences and Health Sector : The Braband region and its diverse and industry driven ecosystem







Corporate and larger companies Presence

Pharmaceutical industries developing their own innovative biopharmaceuticals



SMEs in Advanced therapies and/or biopharmaceutics









Strategic service providers such as CROs and CDMOs







Brabant biopharmaceutical research campus Pivot Park

Research and development in biotech, in particular, has grown rapidly, the report shows. The number of sites grew by 43% and the number of jobs almost tripled (+260%). "This spectacular growth is largely due to the success of the Brabant biopharmaceutical research campus Pivot Park and its neighbours MSD (Merck) Pharmaceutical Operations and Biologicals and Aspen. In 7 years time, Pivot Park, built on the foundation of Organon Research, has grown into the home of 60 biopharmaceutical research companies and institutes with almost 600 employees."

Health, Safety Inbound Fundamental Product Product Marketing & Outbound & Efficacy Manufacturing Logistics Approval Research Development Sales Logistics Research AMGEN Cytura Therapeutics Glycostem Charles Rivers InnSense Aspen AMGEN AMGEN Laboratories Abbot Logistics ImmunoPrecise Lead Pharma Janssen-Cilag MSD (Merck) Janssen-Cilag Abbott Logistics BioFacilities, Landerd **Biologicals &** Citryll Synnafix Zwiers Regulatory Covetrus Animal Thermo Fisher Campus Pharmaceutica Consultancy Health Scientific / Patheon Thermo Fisher Certara NTRC Operations Scientific Janssen-Cilag MSD (Merck) MSD (Merck) Animal Softgels Acerta Pharma Acerta Pharma MSD (Merck) Animal Venn Life Sciences Alliance Healthcare Medtronic (AstraZeneca) (AstraZeneca) **Biologicals &** Health Health Pharmaceutical Brocacef Edwards Life Sciences Brocacef •7immer Biomet Operations AMGEN Global SSC Ardena Centrafarm / STADA Philips Healthcare Philips Healthcare MSD (Merck) Animal Agglomix Hollister •Zimmer Biomet Thermo Fisher VDL ETG, Enabling Health Dechra Global SSC Scientific Electron Philips Healthcare Philips Healthcare **Technologies Group** Pharmaceuticals **Microscopy Solutions** Hollister Thermo Fisher •GE Healthcare Life Medtronic Philips Healthcare DEMCON Scientific Electron Sciences Core Imaging •Össur B. Braun Medica •Thermo Fisher Philips Healthcare •GE Healthcare Life Illumina Boeren Medical Scientific Electron Thermo Fisher Sciences Core Imaging •DEMCON Illumina Adimed Microscopy Solutions Scientific Electron Xeltis •GE Healthcare Life Red text = (Bio)Pharma Malvern Panalytical Ventinova Medical •GE Healthcare Life Microscopy Solutions VanBerlo Agency Sciences Core Imaging Black text = MedTech or GCX Corporation Blue Medical Devices Sciences Core Imaging •GE Healthcare Life MedTech and (Bio)Pharma Hendrix Genetics •Össur / Welling Sciences Core Imaging MicroSure MicroSure MedEve •Össur Preceves Preceves •DEMCON Support industry & services: HR, Finance, IP, IT, Certification, Packaging, Infrastructure etc. Systemair – Tjoapack – Sioux Embedded Systems – Omron – Neways Technology – Thales Cryogenics – IT&Care – STERIS / Synergy – Arnold & Siedsma – PerkinElmer / One Source Outsourced services: logistics (3PL, 4PL); research (CRO); manufacturing (CMO); sales (agents & distributors) BioConnection - Rhenus - Ardena - O&M Movianto - Pivot Park Screening Centre - DB Schenker Healthcare Hub - ImmunoPrecise - HealthLink - Eurofins / Spinnovation Analytical Universities & Knowledge Institutes Radboud University Medical Center (Nijmegen) - TU/e. Eindhoven University of Technology - JADS, Jheronimus Academy of Data Science (a.o. Den Bosch) - Avans University of Applied Science (a.o. Breda) - Fontys University of Applied Science (a.o. Eindhoven, Den Bosch) - Holst Centre (Eindhoven)

The Integrated Value Chain Life Sciences & Health Brabant, including a selection of companies

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Access to Finance

From the "Unlocking the life sciences potential -Key drivers to fully harvest the life sciences sector potential in the Netherlands - KPMG 2019"

- Public and private capital has been readily available in the Netherlands, with a primary focus on pre-seed, seed and expansion (and sometimes later) stages (up to approximately €50 million)
- life sciences companies often look internationally for funding, especially in later stages, as Dutch investors typically lack scale for late-stage investments.
- Public funding in the Netherlands is often provided in the form of loans

- × <mark>></mark>	Year	Fund raised	Description
ápa gos	1999	-	Founded
Overview of	2002	23.3	Private placement in NL
funds raised	2003	22.3	IPO, Euronext Brussels
by Galapagos	2007	4.4	Equity investment by GSK
since its	2013	279.0	IPO, Nasdq (US)
founding	2019	1,110.0	Gilead equity investment





Figure 5. Funds raised by top Dutch-based life sciences focused investors between 2015 and 2019⁴⁹



Funded by the European Union

Galá

Use case – Netherlands Centre for the Clinical advancement of Stem Cell and Gene Therapies (NECSTGEN)

A collaborative approach towards biomanufacturing facilities

Located in Leiden BioScience Park

State of the art GMP facility and expert knowledge for the development, production, and commercialization of cell and gene therapies

NECSTGEN is a non-profit spin out of Leiden University Medical Center (LUMC) located in a purpose-built facility on the largest bio-cluster in the Netherlands, Leiden Bio Science Park (LBSP).

The facility will act as a hub to foster public-private interaction within the cell and gene therapy community, creating a network to link relevant stakeholders, therapy developers, service providers, government, regulators and investors.

NECSTGEN













Part VI

Conclusions and

next steps The Netherlands





Conclusions & next steps

The success of the Dutch R&D model is characterized by

- Strong partnerships with Industry at Educational level (collaborative campus schemes)
- Collaborative model for the Dutch Centres for Entrepreneurship
- National Strategy for innovation and talent
- Attractiveness of the Dutch university and education system
- Cross-sectorial collaboration (i.e AgroFood)
- Digital hub and Digital Innovation Hubs
- One of Europe's largest start-up ecosystems
- High level of **public-private partnerships**

Next steps are:

- To work on solutions to overcome the highly fragmented and competitive own LifeScience environment
- To get access to European and Private fundings to not only stimulate development of disruptive innovations in sector but also to actively fund the growth and scale up of the companies in Europe for this very innovative industrial sector





EIT Health network footprint in the Netherlands

- 1. Industry
- 2. CDMO
- 3. Academic
- 4. Innovation
- 5. Start-ups & Investors

Scoring - Partners engagement with EIT Health





Funded by the European Union

References



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• Europe's first AI lab for bioscience to accelerate innovation

27-Jan-2021 By Lynda Searby

New Artificial Intelligence (AI) applications in the biomanufacturing of food enzymes and dairy cultures will be among the innovations to come out of a new lab that is being established in the Netherlands.

Improving patient access to gene and cell therapies for rare diseases in Europe.

A review of the challenges proposals for improving patient access to advanced therapeutic medicinal products in the Netherlands. Eurordis/Dolon

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A strong foundation for growth and innovation European companies have an opportunity to play a stronger role in the industry by focusing on three factors. Franck Le Deu and Jorge Santos da Silva – McKinsey & Company report

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- Holland Bio data base: Dutch Life Science Database HollandBIO
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