



Annual Report

2021

SkylineDx Holding B.V.
Rotterdam

SKULLINER

I. Annual Report

1

1. Introduction

1.1 The Year of 2021

“2021 was a transitional year. SkylineDx is always focused on precision medicine through re-search and development of molecular diagnostics; today, we are also increasing and dedicating our efforts in bringing our tests to the clinic in the United States of America (US) and the rest of the world. This adds experience and growing expertise in market access and reimbursement to our profile. Our first products are in-market now, and more will follow in 2022 and beyond! For the benefit of patients, and to generate sustainable revenue streams for our investors. Let us show you how we did this, in this new, interactive Annual Report.”

Dharminder Chahal, CEO SkylineDx



2. Our metrics for success: Access for patients and cooperation with partners

2.1 We put patients first

The medical needs in SkylineDx' three focus areas are substantial:

Kawasaki Disease (KD) is a rare, acute inflammatory disease with unknown origin that causes inflammation of arteries, particularly in the heart, and predominantly affects infants and children below 5 years of age.

Epidemiology¹:

Japan: 359/100.000;

South Korea: 197/100.000;

China: 45/100.000;

Taiwan: 57/100.000

USA: 21/100.000;

Europe: 10/100.000

*kids under age of 5.

Multiple Myeloma (MM) is the second most common hematologic malignancy.

Epidemiology²:

Global: 7/100.000;

Skin cancers (Melanoma and Squamous Cell Carcinoma, SCC)

Melanoma is a type of skin cancer that develops when melanocytes (the cells that give the skin its tan or brown color) start to grow out of control.

Squamous Cell Carcinoma (SCC) is a common type of skin cancer that can develop from a pre-cancerous skin growth called an actinic keratosis.

Melanoma epidemiology³:

Global: 5/100.000;

Squamous Cell Carcinoma epidemiology⁴:

Global: 70/100.000;

Kawasaki Disease Reference: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5856963/> en PPT

Multiple Myeloma Reference: <https://gco.iarc.fr/today/data/factsheets/cancers/35-Multiple-myeloma-fact-sheet.pdf>

Melanoma Reference: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5575560/>

Squamous Cell Carcinoma Reference: <https://jamanetwork.com/journals/jamadermatology/fullarticle/2767662>

The number of patients in these three disease areas vary per region around the globe. In general, numbers are increasing for all these conditions.

Use of diagnostics in an early stage is of great importance to craft ideal care pathways for the individual patient. *That is why access to molecular diagnostics is key and will benefit all patients.*

We thank the patients participating in our R&D programs. In fact, they facilitate innovation for other patients:

Falcon R&D Program

Falcon R&D Program in Dermatology.

In 2021, 958 patients participated in melanoma trials (Merlin Test: 748; Peregrine Test 210 pts). This generated 2 scientific publications, and 4 abstract presentations at medical congresses.



Panthera R&D Program in Hematology.

1,071 patients participated in multiple myeloma trials. This generated 7 scientific publications and 4 abstracts on medical congresses that included SKY92.



Delphia R&D Program in Infectious & Inflammatory Diseases.

In October 2021, a collaboration agreement was signed with Imperial College London. After they've dedicated years of research on a gene signature for Kawasaki Disease, SkylineDx will develop it in a near-patient test.



Strix Biomarker Discovery Service.

Data from 74,373 kidney disease patients were analyzed to find markers that facilitate early detection of acute kidney injury. The results are reported in a scientific publication.

Over 30 independent authors contributed to the scientific publications that were published in 19 high-standing medical journals and global congresses.

The road to the patient

Stepping stones from discovery to clinical use and commercial success of our diagnostic are:

Discovery > Development > Validation > Market Access.

Often, this last phase includes marketing authorization.

Current status, depending on geography

Market Access:

Multiple myeloma SKY92 test (prediction of early relapse) on microarray is available for patients in both Europe and USA.

A milestone in creating access to our test portfolio has been achieved through the first commercial payor coverage agreements in USA and outside the USA through several international insurance companies.

Market Access:

The Merlin Test (safely forgo sentinel lymph node biopsy surgery in melanoma) is available for patients in the USA.

Validation phase:

Merlin Test is in validation phase in Europe (pre-marketing authorization) and therefore not yet available for patients.

Peregrine Test (prediction of melanoma recurrence in sentinel lymph node negative patients) is in validation phase for both geographies.

In Development phase:

SKY92 classifier on another technical platform (RNAseq)

The Merlin Test on Idylla (Biocartis collaboration)

PCL-like classifier in multiple myeloma (subgroup of MM patients for whom the disease behaves like plasma cell leukemia)

Kestrel Study Initiative:

Predictive marker to identify early-stage melanoma patients at high risk of distant metastasis

Alopex Study Initiative:

Predictive marker to identify the high-risk squamous cell carcinoma patient and aggressive tumors.

2.2 Collaborative partnerships

We are in collaborative cooperation with numerous academic and commercial institutions. In all phases of development, securing our future pipeline: from discovery to market access strategies.

Discovery:

Scouting candidate biomarkers: a 3-year strategic partnership with VIB (Belgium) was announced December 2021. We will jointly evaluate opportunities regarding novel molecular diagnostics

Strengths combined:

VIB: expertise in state-of-the-art single-cell analysis and biomarker discovery applied to molecular pathology and precision diagnostics

SkylineDx: strategic expertise, global network of renowned clinical centers and physicians, and know-how in the development, market access and early commercialization of in vitro diagnostics.

Development:

Translational science: February '21 a license agreement was signed on a shared patent covering an innovative algorithm for biomarker research in oncology. This algorithm is able to identify subgroups of patients that will benefit more than the population as a whole from a certain cancer treatment. Partners are Oncode Institute and Utrecht Holdings in the Netherlands.

Strengths combined:

Oncode Institute: unites over 900 oncology researchers at 12 Dutch institutes and actively invests in scientific excellence, collaboration and valorization. This accelerates the translation of breakthrough discoveries into tangible benefits for patients and society at large.

Utrecht Holdings (subsidiary of the University Medical Center in Utrecht (UMCU) and Utrecht University (UU)): facilitates the valorization of UU and UMCU founded innovations and intellectual property (IP), making science actually benefit the patient. Invests in promising spin-offs based on scientific discovery from or related to both institutions.

SkylineDx: apply academic outcomes in support of (bio)pharmaceutical development. Tailor cancer research to specific patient needs through the STRIX Biomarker Discovery Service by utilizing basic academic research as a foundation for further development.

Validation:

Confirmation of performance: on 30 April '21 the performance of our melanoma diagnostic test (Merlin Test) was confirmed in a group of USA patients from the Mayo Clinic and West Virginia University. The independent publication in the International Journal of Dermatology was important for the ongoing reimbursement strategy and uptake in medical guidelines and standards.

Strengths combined:

Mayo Clinic and West Virginia University: independent clinicians and scientists, access to eligible patients in routine clinical practice, authoring an independent report for peer-reviewed scientific Journal. The partners arranged funding from National Cancer Institute and the National Center for Advancing Translational Sciences in the USA, as well as Mayo Clinic's Center for Individualized Medicine and Mayo Clinic Cancer Center.

SkylineDx: running a field medical and scientific affairs team in the USA and a commercial CAP/CLIA certified laboratory in San Diego (California). Uses its expertise to bridge the gap between academically discovered gene expression signatures and commercially available diagnostic products with high clinical utility, assisting healthcare professionals in accurately determining the type or status of disease or predict a patient's response to treatment.

Market Access:

Commercial development and market distribution: in April '21 a partnership agreement was closed with Biocartis Group, for the development of SkylineDx' novel proprietary test - the Merlin Test -, on Biocartis' rapid and easy-to-use molecular diagnostics platform Idylla™. This assay is aimed at predicting a patient's risk of nodal metastasis in melanoma.

Strengths combined:

Biocartis Group: this innovative molecular diagnostics company (Euronext Brussels: BCART) will lead the commercialization in Europe through its growing network.

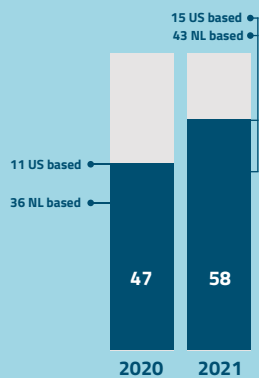
SkylineDx: will lead the development of the Merlin Test on the Idylla™ platform.

2.3 A strong team

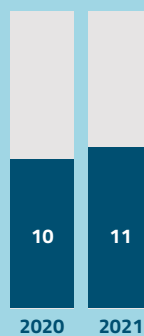
Our Team expanded over 2021 in many aspects, both in R&D and commercial functions:



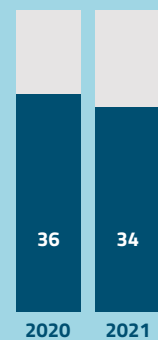
Headcount



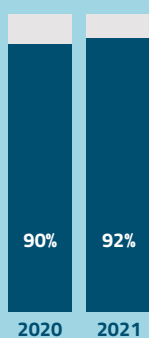
Nationalities



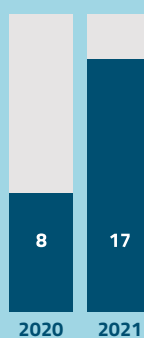
Average age



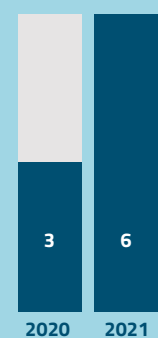
Academic level degree



New staff



Positions vacant



Skilled and dedicated:

CAP Accreditation.

A thrilling example of dedication and excellence of our team was the renewed accreditation to SkylineDx' laboratory in San Diego, California (USA) by the International the Accreditation Committee of the College of American Pathologists (CAP), November 2021.

The USA federal government recognizes the CAP Laboratory Accreditation Program as being equal-to or more-stringent-than the government's own inspection program. CAP inspectors also examine laboratory staff qualifications, equipment, facilities, safety program and records, and overall management. Our team in San Diego did an incredible job anticipating CAP's on-site inspection, further solidifying our position in the USA diagnostics market.

ISO certification.

Another proof for our team's skills was the esteemed ISO 13485:2016 Quality Management System certificate we received in February '21. This internationally recognized standard of excellence is a stringent guideline for medical device manufacturers to address the regulations, responsibilities and demonstrate the commitment to the safety and quality of the developed medical devices. To achieve this certification, our team had to demonstrate consistent de-sign, development and servicing of their molecular tests, that they are safe and ef-fective for their intended purpose.

2.4 Added value, backed by loyal investors

Investments in SkylineDx took an international scope in 2021. Now that the products are solidi-fying their footprint on the USA market, we received the commitment for a capital investment from USA based investment and advisory firm Novalis LifeSciences, and one of Benelux' largest biotech investors Van Herk Royalty. This backing by Novalis is particularly important as this is a reputable diagnostics biotech investor, and this investment also includes a supervisory board position.

Aim is to further expand our position in the USA dermatology diagnostics market:

SkylineDx' dermatology program, often referred to as the Falcon R&D Program, current-ly overarches four dedicated dermatology initiatives, focused on prognostic and predic-tive biomarker development covering two skin cancers: melanoma and squamous cell carcinoma. These indications affect approximately 1.9 million patients annually in the USA only.

One of these initiatives generated its first commercially available product, branded as Merlin Test, for which SkylineDx aims to accelerate the clinical adoption with this joint investment.

Marijn E. Dekkers, founder and chairman of Novalis LifeSciences, commented:

"I have monitored the progress of SkylineDx for several years now, and I am excited about the leading edge position the company has built in predictive biomarkers for melanoma and various other cancers. I very much look forward to working with the SkylineDx team to bring these sophisticated diagnostic tests to patients around the globe".

We invest ourselves in promising projects, too. June '21 we announced to co-invest in research and development in the field of Squamous Cell Carcinoma (SCC), as part of a Dutch consortium including the Erasmus MC Cancer Institute and University Medical Center Rotterdam (EMC):

- The collaboration focuses on the discovery and validation of a model that identifies the SCC patient at high risk of developing metastasis. These high-risk patients would benefit from an intensive surveillance program to closely monitor the progress of their disease.
- The second objective is to enrich the model by adding genomic information to identify the most aggressive tumors among high-risk patients. Those patients may benefit from more aggressive or adjuvant treatment to reduce their risk of metastasis.
- This is to create predictive models that can differentiate these patients with a good prognosis from the patients at high risk of developing metastasis.

I. 3.3 Personnel

SkylineDx' relationship with its personnel is good. SkylineDx continuously invests in its personnel through training and development programs. SkylineDx regards the know-how of its personnel as an important strategic asset. The average number of employees of SkylineDx during 2021 was 49 FTE. I would like to thank our people for their continued loyalty and dedication to develop SkylineDx into a company that has high impact on the life of patients it serves through diagnostic services.



I. 3.4 Outlook

We continue to expect further graduate growth in terms of investments in research and development activities as well as the number of employees. Management expects that during the next few years the investment in research, development and commercial development will continue to be significant. Funding of SkylineDx' activities is currently undertaken by our main private investor van Herk Royalty and Novalis Lifesciences.

SkylineDx continues to apply the going concern principle since the company has instituted measures to assure sufficient cash and secure additional finance with the current and new third party shareholders.

Rotterdam, 25 May 2022
On behalf of Exponential B.V.
D.S. Chahal



“It is our dream to improve a patient’s quality of life by enabling them to benefit from personal insights at the genetic level of their disease. It is our dream to make that happen for every patient, for every disease.”

– Dharminder Chahal, CEO of SkylineDx