



Annual Report

2023

SkylineDx Holding B.V.
Rotterdam
July 2024

SkylineDx



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SkylineDx Annual Report 2023

1.1 Introduction

1.1.1 2023: Sharpening our Two-Sided Sword

Continuing our core strategy - combining targeted R&D with a solid marketing strategy and end user involvement – we are well positioned for commercial success. In 2023, major goals were met on both edges of this 'two-side sword'. Outcomes of our groundbreaking research were presented in several scientific papers and at key scientific conferences, while additional market access was granted for our products and services in both US and throughout Europe.

Unlocking presence

Commercialization was driven by expanding our team with experienced business development and marketing experts that could lead our commercial partnerships.

To unlock geographic presence and market penetration across the globe, we developed our marketing entry strategies in cooperation with local partners. Strategic mapping of our partners aims at each of them serving different segments of customers, in a defined region and market opportunity. For example, for our Merlin test, one of our US partners is rooted in academic settings, while our other partner is covering private dermatology practices from coast to coast.

Monetize IP

Moreover, we introduced the first sublicense agreement as a new way of monetization on our IP. Sublicensing allows the customer to benefit from a 'private-label' version of our test technology, carrying the branding of our partner. This new strategy greatly enhances our potential market-span in geographies and client segments where we have limited presence yet. This will surely accelerate the adoption of the test across the US.

Funding secured

While being cost conscious as always, we secured several grants for funding clinical development projects that connect seamlessly with our well-known R&D-programs like Panthera, Falcon and Delphia.

Our science and our scientists have been more and more visible in the biotech ecosystem, as we pinpoint on external focus and communications more than ever. That visibility and awareness is a critical factor in gaining traction for continuity and growth. The investors community is risk averse nowadays, so insights and trust is required for them to embrace the dynamics of health economics and biotech. We are working on that external profile as a firm, and this resonates well among our partners.

So, effective R&D and savvy commercialization sharpened our two sided sword over the past year. Dynamics are good, and outlook is promising.

All in all, we are positive towards growth and adding value for the patient, paired with a healthy financial outlook as an established biotech company.

On behalf of the global SkylineDx team,

Dharminder Chahal, CEO SkylineDx



1.1.2 Strategic outline

Our key strategies at a glance



1. Dual Focus: we combine targeted R&D with effective marketing, positioning ourselves for commercial success by achieving major goals in both research and market access.



2. Research Outcomes: significant outcomes from R&D efforts, including numerous publications and presentations at scientific conferences, demonstrate our commitment to innovation and advancement in diagnostics and services.



3. Cost Management and Funding: aside cost consciousness and understanding of investors interests, we aim at grants for clinical development projects, enhancing our renowned R&D programs.



4. Strategic Commercialization: Expansion of the team with experienced business development and marketing experts, further strengthens the company's presence in the diagnostics marketplace. Intense partnerships with local entities facilitate global market penetration and tailored approaches for different customer segments and regions.



5. Innovative Monetization: Introduction of sublicense agreements diversifies our revenue streams. This approach expands the company's market reach, particularly in regions or market segments where our presence is not yet fully developed.

1.1.3. Outlook to 2024 and beyond

In line with the strategy outlined above, in 2024 we expect to be able to achieve important developments in both strategic areas: research and market access.

Merlin: from discovery to reimbursement

A prime example is the Merlin test, our molecular diagnostic tool, designed to provide personalized insights into early-stage melanoma cancer patients' treatment options.

Since the discovery of the model was published, international validation studies and recently a prospective study have consistently demonstrated the strong performance of the test to predict the risk for nodal metastasis.

Early 2022, this clinical evidence enabled Medicare coverage under the MoIDX local coverage determination for Melanoma Risk Stratification. New publications, such as a multicenter study published in October 2023, added data on successful clinical validation and implementation of this clinicopathologic and gene expression profile (CP-GEP) model in the 'real-world'.

Consequently, in December 2023, SkylineDx went into a strategic commercial collaboration with Tempus, a leader in precision medicine, to further roll-out and support the Medicare activities with Merlin. Tempus, renowned for its expertise in leveraging the power of artificial intelligence and data to drive advancements in healthcare, brings its experience and vast commercial network to this collaboration between SkylineDx and Medicare.

Guidelines and reimbursement

In 2024 and beyond, accumulating evidence from research outcomes and real-world data will further boost access and guideline inclusion of our diagnostics.

For example, the read out of MERLIN_001 will be an important step towards NCCN guidelines review. The most recent version of the NCCN guideline for melanoma already cites our prospective trial. That is very positive, as NCCN obviously sees the trial as a crucial milestone in the establishment of clinical utility for GEP to predict SLNB status. It recognizes how a test should be evaluated and how it should demonstrate added value over readily available clinical and pathological features.

Another milestone was the development by Quest Diagnostics of MelaNodal Predict™, their branded version of the Merlin-test, aiding personalized treatment decisions for melanoma, to be launched early 2024. Dermatologists and other providers nationwide may then begin ordering the test from Quest Diagnostics, as well as through DermPath Diagnostics, Quest's subspecialty pathology business.

The collaboration aims to utilize Quest's national scale in the US, and SkylineDx's expertise to enhance melanoma care accessibility. This innovative partnership underscores the transformative potential of collaborations in healthcare, aiming to make a meaningful impact on melanoma patient care.



1.2 Metrics for success

1.2.1 Collaborative partnerships

The Board and directors of SkylineDx recognize the potential for industry-academia collaborations to drive innovation.



SkylineDx and Oncode Institute

Since the first common project in 2021, our established partnership is intensifying with Oncode, an independent Dutch institute dedicated to understanding cancer and translating research into practice. In 2023, Oncode Investigator Miao-Ping Chien (Erasmus MC) in collaboration with SkylineDx received a TKI-LSH PPP Allowance to kickstart a project aimed at investigating the underlying mechanisms that drive metastasis in head and neck squamous cell carcinoma (HNSCC). Currently, the prognosis and the risk stratification of HNSCC patients are insufficient to accurately predict treatment outcomes and survival. This newly funded collaboration aims to find improved biomarkers that can help predict metastasis, and risk-stratify the patients, thus enabling more risk-based design of intervention strategies (e.g., surveillance intensity and immunotherapy eligibility), and improving survival for patients with HNSCC.



SkylineDx and VIB

A significant partnership in advancing healthcare solutions announced in 2023, is POINTILLISM 2.0. The project will analyze blood and tumor samples from cancer patients to explore predictive biomarkers. This represents a pivotal endeavor toward personalized cancer treatment. POINTILLISM 2.0 is a joint research program SkylineDx and VIB have initiated, that was selected for funding through the VIB Grand Challenges Program. Collaborators include VIB, KU Leuven, SkylineDx, and University Hospital (UZ) Leuven, pooling expertise in cancer biology, molecular mechanisms, and tech transfer. This initiative aligns with the societal goal of identifying biomarkers to predict treatment response, thereby reducing adverse events and healthcare costs.

1.2.2 Outcomes in all dimensions

The value and practical feasibility of risk stratification with our diagnostics is true in various indications. Scientific milestones were published in 2023 across our areas of interest. In addition to the achievements already mentioned above, here we summarize some other main outcomes.

Multiple Myeloma – SKY92

At the American Society of Hematology (ASH) 2023 Annual Meeting, findings from the PROspective Observational Multiple Myeloma Impact Study (PROMMIS) trial were presented. Multiple Myeloma (MM) is a complex hematologic malignancy, presents challenges in predicting disease progression and treatment responses. This PROMMIS prospective US multicenter trial, encompassing 251 MM patients, showed that the SKY92 gene expression profiling (GEP) assay's distinguishes MM patients into high-risk and standard-risk groups, aiding in prognosis and treatment planning. This means that integrating SKY92 with conventional risk assessments not only improves risk assessment accuracy but also boosts physician confidence. In addition, findings from the OPTIMUM trial on the efficacy of SKY92 were published at the International Myeloma Society Meeting. The trial, conducted across nearly 40 UK hospitals, combined SKY92 with

standard genetic testing to identify ultra-high-risk MM (UHRMM) patients. These individuals, previously undetected by standard methods, showed improved outcomes (significantly higher progression-free survival (PFS) and overall survival (OS) rates) with intensified treatment. This highlights SKY92's role in supporting personalized treatment protocols, and its clinical utility.



Cutaneous Melanoma – CP-GEP

In dermatology, more specific in Cutaneous Melanoma (CM) patients, the added value of another SkylineDx invention was confirmed in a presentation at the Society for Melanoma Research Congress. A retrospective multicenter study investigated the Clinicopathologic and Gene Expression Profile (CP-GEP) model's

performance in stratifying risk of disease recurrence. Our CP-GEP model demonstrates effectiveness in identifying high-risk Stage I/II CM patients and stratifying Stage III patients. This confirms the model's capacity to optimize patient management, offering refined treatment and surveillance approaches.



1.2.3 Living to our values

In our 'Meet SkylineDx on Friday series', no less than 42 personal stories by SDx colleagues were published throughout 2023 on LinkedIn. This gives a great insight into the motivation and practical challenges of our colleagues.

Personal drivers

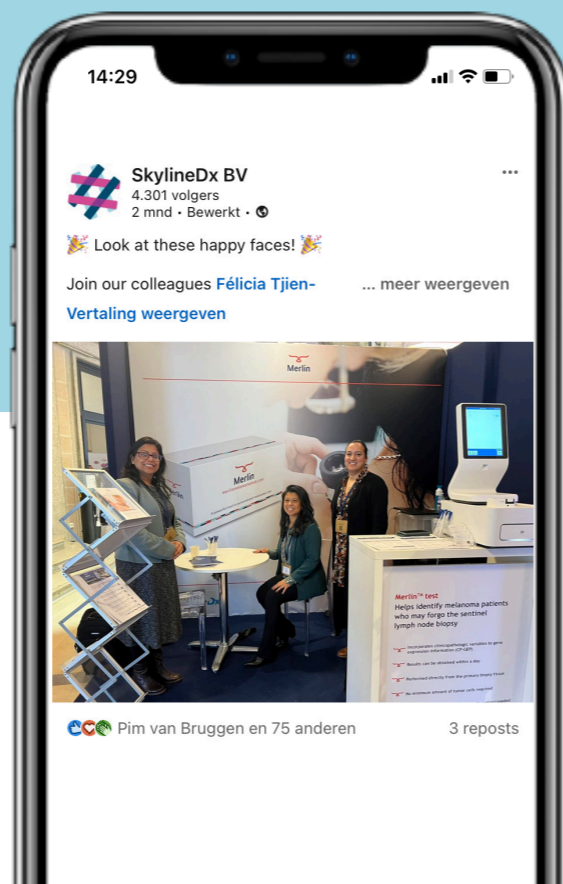
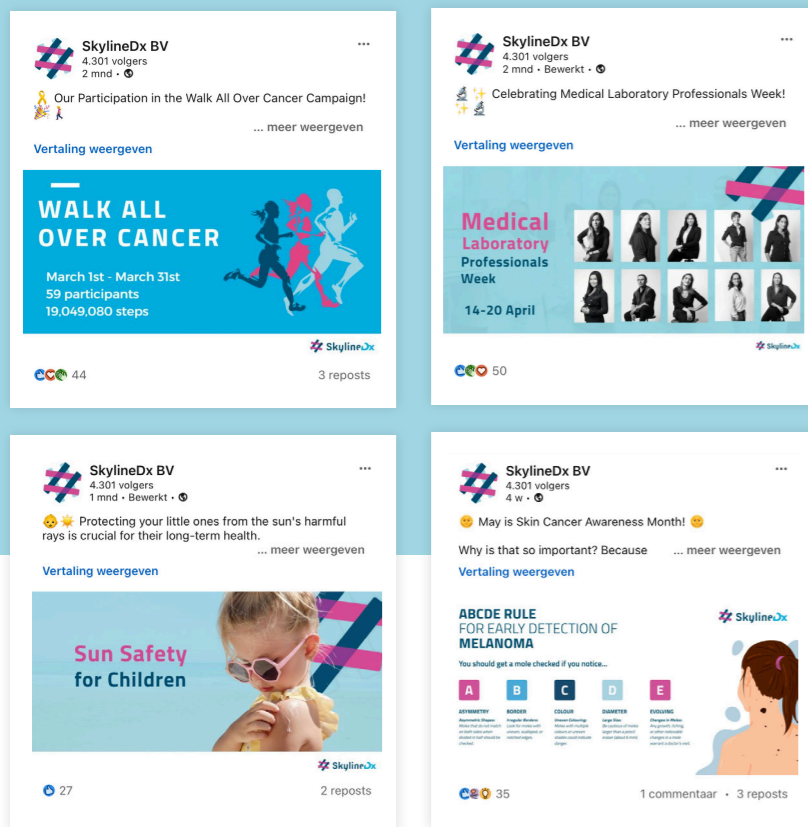
It is impossible to select only a few of these stories to cite in this Annual Report, as all 42 are showing just a shimmering particle of the full spectrum of our essence.

Reading the personal stories, it shows that many employees express a strong passion for science and innovation, driven by their desire to translate scientific knowledge into practical solutions for patients. Across all roles, there is a common commitment to improving patients' quality of life. Employees feel proud to be part of a company that prioritizes patient well-being and strives to make a positive impact in the battle against diseases like cancer, by providing timely treatments to patients.

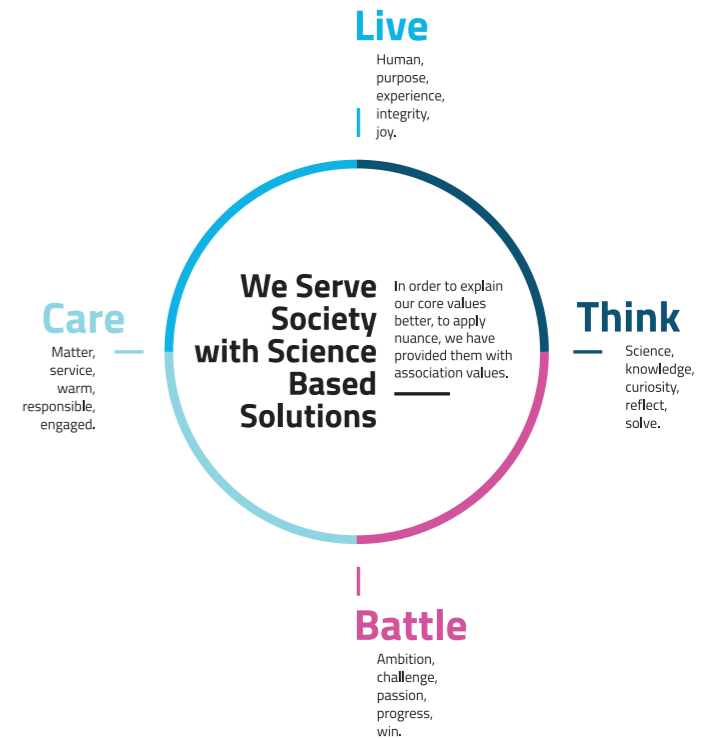
Multidisciplinary Teamwork

Another key observation overlooking the 2023 series, is the value of teamwork and collaboration, emphasizing the importance of working together toward common goals in multidisciplinary teams. Moreover, employees derive a strong sense of purpose from their work, as every task, whether it's developing new products or ensuring quality control, ultimately serves the greater purpose of improving patient outcomes.

Finally, our team recognizes the rapidly changing nature of healthcare and the need for adaptability and resilience. We embrace challenges and demonstrate a willingness to overcome obstacles in pursuit of their goals.



'Living to our values' was also reflected in year-round CSR-initiatives. Our corporate values were connected with several 'World Days', covering a variety of events with both internal and external scope. Some related to illness and health, like World Cancer Day, Melanoma Month and Kawasaki Disease Day. Other events and activities tapped into well-being and responsibility in more general terms, like Earth Hour, International Childrens Day and Positive Thinking Day. Each quarter, employees were selected as "value ambassadors" to drive the initiatives. This notably increased both corporate culture awareness internally, and our company visibility in the outside world.



The four Values that resonate in the personal 'Meet SkylineDx' stories - and that have been our internal compass for several years now - are: to Live, Think, Battle and Care.

- ✓ We live to make a difference.
- ✓ We think about how our innovations can impact many lives.
- ✓ We battle to make progress in a conservative world.
- ✓ We care about the people we serve.

We **LIVE** to make a difference, fueling our passion to drive positive change in healthcare

We **THINK** about how our innovations can impact many lives, constantly seeking new ways to push the boundaries of what's possible

We **BATTLE** to make progress in a conservative world, challenging norms and overcoming obstacles with determination and resilience

We **CARE** about the people we serve, approaching our work with empathy, compassion, and a deep sense of responsibility



2. SkylineDx first decade; ready for the future

As we celebrate the first decade of SkylineDx, we reflect on our journey from a promising startup to an established biotech company. Over these ten years, we have pioneered advancements in diagnostics and personalized medicine, achieved significant milestones, and laid a robust foundation

for future growth. Our unwavering commitment to innovation, strategic partnerships, and patient-centered solutions has positioned us at the forefront of the biotech industry.

Visor Company - SkylineDx

3. Conclusion

As we embark on the next chapter of our journey, SkylineDx is well-prepared to navigate the future of healthcare with confidence and determination. Our first decade has been marked by remarkable achievements, and we are excited about the opportunities that lie ahead. "Our commitment to innovation and patient-centric solutions has been the cornerstone of our success. As we look to the future, we remain dedicated to transforming diagnostics and improving patient outcomes worldwide," Dharminder Chahal, CEO SkylineDx

With a strong foundation, a clear vision, and an unwavering dedication to excellence, SkylineDx is ready to embrace the challenges and opportunities of the future, driving advancements in diagnostics and making a lasting impact on global healthcare.

See how we have rocketed to new heights

