Report on Risks and Opportunities

Risks and opportunities are an integral part of our entrepreneurial activities. Merck has put responsibilities, processes and tools in place to identify risks at an early stage and mitigate them by taking appropriate action. Within the company, risk and opportunity management is a core component of our internal business planning.

Risk and opportunity management

Merck operates in a complex, global business world and is exposed to a wide range of external and internal influences. Every business decision is therefore based on the associated risks and opportunities.

In our internal risk reporting, risks are defined as potential future events or developments that could lead to a negative deviation from our (financial and non-financial) targets. In parallel, opportunities imply a positive deviation from our planned targets. Identified future events and expected developments are taken into account in internal planning, provided that it can be assumed that their occurrence is likely in the planning period. The risks and opportunities presented in the risk and opportunities section are those potential future events or developments that could respectively lead to a negative or positive deviation from existing plans.

Risk management process

The objective of our risk management activities is to identify, assess, and manage risks early and to implement appropriate measures to reduce them. The responsibilities, objectives, and processes of risk management are described in our internal risk management guidelines. The business heads, managing directors of Merck subsidiaries, and the heads of Group functions are specified as employees with responsibility for risks. The risk owners regularly assess their risk status and report their risk portfolio to Risk Management. We use special risk management tools to support these activities.

In this context, risk-mitigating measures are evaluated. The effectiveness of these measures and the planned implementation time frame are monitored and the residual risk is presented in the internal risk report as net risk.

Group Controlling & Risk Management forms the organizational framework for risk management and reports directly to the Group Chief Financial Officer. Within the scope of audits, Group Internal Auditing regularly reviews the performance of risk management processes within the units and, at the same time, the communication of relevant risks from the operating businesses to Group Risk Management. Furthermore, the external auditor reviews the risk early warning system in the course of its annual audit of the financial statements. Group Risk Management uses the information reported to determine the current risk portfolio for the Merck Group, presenting this in a report to the Executive Board, the Supervisory Board, and relevant Committees with detailed explanations twice per year. This also encompasses a quantitative aggregation of risks at Group level, using a Monte Carlo simulation. Furthermore, significant changes in the assessment of the risks already known and new significant risks can be reported at any time and are communicated to the Executive Board on an ad-hoc basis.

For the internal bottom-up risk reporting process, a minimum threshold of a potential negative impact on our EBITDA pre is set at the level of € 10 million in the standard cycle and € 25 million in the ad-hoc process. The timeframe applied for internal risk reporting is five years. It can go beyond five years in special cases, e.g., for regulatory risks related to climate change. The outlined risks and their evaluation are based on respective annual values in the reporting timeframe. The assessment of the risks presented relates to December 31, 2021. There were no relevant changes after the balance sheet date that would have necessitated an amended presentation of the risk situation of the Group.

Opportunity management process

The opportunity management process is integrated into our internal controlling processes and is carried out in the operating units on the basis of the Group strategy. The businesses analyze and assess potential market opportunities as part of strategy and planning processes. In this context, investment opportunities are examined and prioritized primarily in terms of their potential value proposition, in order to ensure an effective allocation of resources. We specifically invest in growth markets to leverage the opportunities of dynamic development and customer proximity at a local level.

If the occurrence of the identified opportunities is rated as likely, they are incorporated into the business plans and the short-term forecasts. Trends going beyond this, or events that could lead to a positive development in the net assets, financial position, and results of operations, are presented in the following report as opportunities. These could have a positive effect on our medium-term prospects.

Risk and opportunity assessment

Risks

The significance of risks is calculated on the basis of their potential negative impact on the forecasted financial targets in conjunction with the probability of occurrence of the respective risk.

The underlying scales for measuring these factors are shown below:

Probability of occurrence

Probability of occurrence	Explanation
< 1%	Highly improbable
1 – 5%	Improbable
5 – 20%	Possible
20 – 50%	Likely
> 50%	More than likely

Degree of impact

Degree of impact	Explanation
> € 500 million	Critical negative impact on the net asset, financial position, and results of operations
€ 100 – 500 million	Substantial negative impact on the net asset, financial position, and results of operations
€ 25 – 100 million	Moderate negative impact on the net asset, financial position, and results of operations
€ 10 – 25 million	Minor negative impact on the net asset, financial position, and results of operations
< € 10 million	Immaterial negative impact on the net asset, financial position, and results of operations

Opportunities

Opportunities are assessed in their respective specific business environment. General measures of the business functions are quantified during operational planning, usually in relation to sales, EBITDA pre, and operating cash flow. Net present value, internal rate of return, the return on capital employed (ROCE), and the payback period of the investment are primarily used to assess and prioritize investment opportunities. We use these indicators to assess the opportunities arising from the investment projects. Similarly, scenarios are frequently set up to simulate the influence of possible fluctuations and changes in the respective parameters on results. An overarching, systematic classification of the probability of occurrence and impact of opportunities is not carried out.

Internal control system for the (Group) accounting process

The objective of the internal control system for the accounting process is to implement controls that provide assurance that the financial statements are prepared in compliance with the relevant accounting laws and standards. This system covers measures designed to ensure the complete, correct, and timely conveyance and presentation of information that is relevant for the preparation of the Consolidated Financial Statements and the Combined Management Report.

Key tools

Our internal control system for financial reporting is based on the COSO framework, a globally recognized standard divided into five components: control environment, risk assessment, control activities, information and communication, as well as monitoring activities. Each of these components is regularly documented, tested and/or assessed.

The internal control system aims to ensure the accuracy of the consolidated accounting process through functioning internal controls with reasonable assurance. The Group Accounting function centrally steers the preparation of the Consolidated Financial Statements of Merck KGaA as the parent company of the Merck Group. This Group function defines the reporting requirements that all Merck subsidiaries must meet. At the same time, this function steers and monitors the scheduling and process-related requirements of the Consolidated Financial Statements. Group Accounting centrally manages all changes to the equity holding structure and correspondingly adapts the Group’s scope of consolidation. The proper elimination of intragroup transactions within the scope of the consolidation process is ensured. Group-wide accounting guidelines form the basis for the preparation of the statutory financial statements of the parent company and of the subsidiaries, which are reported to Group Accounting; the guidelines are adapted in a timely manner to reflect changes in the financial regulatory environment and are updated in accordance with internal reporting requirements. For special issues, such as the accounting treatment of intangible assets within the scope of company acquisitions or pension obligations, external experts are additionally involved where necessary.

The individual companies have a local internal control system within a global framework. Where financial processes are handled by a Shared Service Center, the internal control system of the Shared Service Center is additionally applied. Both ensure that accounting complies with IFRS (International Financial Reporting Standards) and with the Group accounting guidelines.

Group Accounting provides support to the local contacts and ensures a consistently high quality of reporting throughout the entire reporting process.

For Group financial reporting purposes, most of our subsidiaries use standard SAP software. Consolidation software from SAP is also used for the elimination of intragroup transactions. A detailed authorization concept ensures the separation of duties with respect to both single-entity reporting and the Consolidated Financial Statements. The accounting process is generally designed to ensure that all units involved adhere to the principle of dual control.

The operational effectiveness of our internal control system is regularly tested in the format of self-assessments by our legal entities, group functions, and shared services. The quality is systematically reviewed by a dedicated global financial control and governance team. Control deficiencies are properly recorded and, where necessary, adequate countermeasures are taken to remediate control deficiencies in a timely manner.

The overall effectiveness of Merck's internal control system with regard to accounting and compliance with financial reporting on the part of the individual companies is confirmed by both the local managing director and the local chief financial officer by signing the single-entity reporting and a separate confirmation regarding the effectiveness of the financial control system (internal control system sign-off letter). For the accounting treatment of balance sheet items, Group Accounting closely cooperates with Group Risk Management to correctly present potential risks in the balance sheet.

All structures and processes described related to the Group accounting procedures are subject to regular review by Group Internal Auditing based on an annual audit plan set out by the Executive Board.

The results of the self-assessments, quality reviews, and internal audits are dealt with by the Executive Board, the Supervisory Board, and the Audit Committee. The internal control system at Merck makes it possible to lower the risk of material misstatements in accounting to a minimum. However, no internal control system can entirely rule out a residual risk, whatever its design.

Business-related risks and opportunities

Political and regulatory risks and opportunities

As a global company, we face political and regulatory changes in a large number of countries and markets.

Risk of more restrictive regulatory requirements regarding drug pricing and reimbursement

In the Healthcare business sector, the known trend toward increasingly restrictive requirements in terms of drug pricing, reimbursement, and the expansion of rebate groups is continuing. Specifically, in the United States, a pricing reform on prescription drugs is part of the agenda of the current administration. These requirements can negatively influence the profitability of our products, as can market referencing between countries, and the success of market launches. Foreseeable effects are taken into account as far as possible in the business sector's plans. Close communication with health and regulatory authorities serves as a preventive measure to avert risks.

Remaining risks beyond the current plans resulting from restrictive regulatory requirements are likely with a potential moderate to substantial impact.

Risk of stricter regulations for the manufacturing, testing, and marketing of products

We must adhere to a multitude of regulatory requirements regarding the manufacturing, testing, and marketing of many of our products. Specifically, in the European Union, we are subject to the EU chemicals regulation REACH. Similar regulations are emerging globally in relevant markets, in particular in Asia. These regulations demand comprehensive tests for chemicals. Moreover, the use of chemicals in production and final products could be restricted, which would negatively impact the ability to manufacture and market certain products. With the EU Chemicals Strategy for Sustainability, an initiative of the European Green Deal, we have to expect even increasing demands concerning the substitution of specific hazardous substances. We are constantly pursuing research and development in substance characterization and the possible substitution of critical substances so as to mitigate this risk. Nevertheless, it is classified as a possible risk with a potential substantial impact on the net assets, financial position, and results of operations.

Risk of negative political and macroeconomic developments

The ongoing general trend of de-globalization and reshoring critical supplies might initiate the (re-)establishment of trade barriers, sanctions, and foreign exchange policy changes. Additionally, there is an increasing threat from armed conflicts. These risks can have a negative impact on our supply chains and can lead as well to declines in sales in certain countries and regions. They are taken into account as much as possible in the business plans of the affected countries and regions, and are mitigated through product, industry, and regional diversification as well as measures to ensure resilience of supply chains and networks.

Potential negative macroeconomic developments can also impact our business. To minimize these impacts, corresponding measures pertaining to the sales strategy have been initiated in these countries.

The spread of the coronavirus since the beginning of 2020 is associated with risks in global macroeconomic developments, likewise with the potential for negative effects on our businesses. The opportunities in connection with combating the Covid-19 pandemic are described in the "Market risks and opportunities" section.

The rise in inflation in the course of 2021 across some of our major markets could negatively impact our business. The current inflation dynamics are driven by a combination of base effects, supply disruptions, hefty fiscal spending, and special factors. Persistently high inflation could increase our operating expenses (e.g., raw materials, utilities, and logistics) as well as capital expenditures, and lead to an increase in central bank rates, which would affect our refinancing costs.

The net risk of negative geo-political and macroeconomic developments is seen as possible and might have substantial to critical effects on the net assets, financial position, and results of operations.

Market risks and opportunities

We compete with numerous companies in the pharmaceutical, chemical, and life science sectors. Rising competitive pressure can have a significant impact on the quantities that can be sold and prices attainable for our products.

Opportunities in connection with combating the Covid-19 pandemic

As a science and technology company, we are contributing to the global fight against Covid-19. In Life Science, we have been working with more than 80 vaccine developers around the world and have supported more than 35 testing solutions and more than 50 projects involving monoclonal antibodies, plasma products, and antiviral drugs. We are collaborating with numerous researchers and institutions to assist them with the process development of and the production process for marketed and potential Covid-19 vaccine candidates, as well as for the mass production of SARS-CoV-2 diagnostic tests.

Opportunities from leveraging the e-commerce and distribution platform

In the Life Science business sector, our dedication to the customer experience extends from the lab to our primary e-commerce platform, sigmaaldrich.com, which connects scientists in nearly every country around the world with the products, publications, and technical expertise needed to advance their discovery, research, and development further and faster.

Our efforts include innovative approaches across the globe, bolstering sigmaaldrich.com and our e-commerce expertise. To that end, this year we launched a new website architecture and user interface providing customers with an updated look and feel, enhanced mobile capabilities, and faster and more reliable website performance, as well as features like self-serve order status and product ratings and reviews. In alignment with our long-term e-commerce strategy to leverage sigmaaldrich.com as a scalable growth driver and the destination for our life science community, we are leveraging our new website architecture so that we may continue to improve the customer experience more rapidly and flexibly in the future.

Opportunities presented by viral vectors and HPAPIs/ADCs

In the Life Science business sector, we strengthened our viral vector manufacturing capabilities with the launch of the VirusExpress™ lentiviral production platform. We are committed to accelerating the manufacture of cell and gene therapies with the goal of getting these lifesaving treatments to patients faster. This proven, scalable platform increases dose yields and reduces process development times.

We also expanded our manufacturing capabilities of high-potent active pharmaceutical ingredients (HPAPI) and antibody drug conjugates (ADC) in the United States with the creation of one of the largest single-digit, nanogram containment production facilities for HPAPIs. This will allow the continuous manufacturing of increasingly potent agents at an industrial scale for therapies with the potential to treat cancer. ADCs are an emerging class of medicines designed for the high-specificity targeting and destruction of cancer cells while preserving healthy cells. Only nine ADCs are currently approved worldwide. The ADC industry is experiencing strong growth and is expected to reach € 13 billion by 2030.

Opportunities in the semiconductor industry

We have huge growth opportunities in the semiconductor market due to the significantly accelerating global demand for innovative semiconductor materials. This demand is driven by exponential data growth and highly impactful technology trends such as the Internet of Things (IoT) and 5G. We are working on nearly all of these new technology inflection points of the semiconductor roadmap together with our customers. Our capacity investments are synchronized to our customers' expansion plans and we continue to tackle industry challenges as well as supply reliability. Our semiconductor business has a very broad and unique portfolio which is not dependent on a single product or technology. It consists of different, independent technologies: Thin Film, Patterning, Planarization, Specialty Gases and Delivery System & Services. There is a natural hedge due to our holistic capabilities. Furthermore, we supply products for all essential production steps of wafer processing: patterning, deposition, planarization, etching, cleaning, doping and packaging. For instance, this year we launched the new AZ® 910 Remover which offers an innovative, cost-effective solution to support our customers with their advanced cleaning needs integral to realizing next-generation chips.

Moreover, we are developing new dielectric platforms in cooperation with our key customers for 3D NAND applications. There has been a change in 3D NAND device architecture and some of our customers are moving from floating gate to replacement gate technology. Therefore, we are currently working with these customers on this new device architecture.

Opportunities due to new technologies in the manufacturing of displays

We see major opportunities in significant market growth of organic light-emitting diode (OLED) materials in high-quality display applications. We have been performing research and development in the area of organic light-emitting diode (OLED) technology for more than 15 years and have become one of the leading material suppliers for OLEDs. Through our semiconductor and display knowledge, we will be able to contribute to the new generation of optimized sensors. Furthermore, we see opportunities in foldable displays, which require a broad set of materials ranging from encapsulation to the OLED stack.

Opportunities in liquid crystal distribution

We are pursuing a strategy of leveraging our expertise as the global market leader in liquid crystals in order to develop new fields of application for innovative liquid crystal technologies. Beside the opportunities for displays e.g., for gaming applications, we are pressing ahead to capture the future markets for liquid crystal in windows (LCWs) and mobile antennas. With our smart antenna technology, we offer a unique technology that can be used for the data transfer to the growing number of LEO satellites, providing internet connection to remote areas worldwide. LCWs are creating new architectural possibilities for switchable solar shadings and – as introduced in 2021 - for creating private spaces in public and commercial venues.

Risks due to increased competition and customer technology changes

In the Healthcare business sector, both our biopharmaceutical products and classic pharmaceutical business are exposed to increased competition from rival products (in the form of biosimilars and generics). In the Life Science and Electronics business sectors, risks are posed by not only cyclical business fluctuations but also changes in the technologies used or customer sourcing strategies. We use close customer relationships and in-house further developments as well as market proximity, including precise market analyses, as mitigating measures. Overall, the risk is likely with a potential substantial to critical impact.

Risks and opportunities of research and development

For us, innovation is a major element of the Group strategy. Research and development projects can experience delays, expected budgets can be exceeded, or targets can remain unmet. Research and development activities are of special importance to the Healthcare business sector. In the course of portfolio management, we regularly evaluate and, if necessary, refocus research areas and all R&D pipeline projects. Alliances with external partners and the out-licensing of programs also form part of the catalog of measures for the efficient allocation of resources. The conclusion and continuation of these partnerships and externalizations plays an important role.

The strategic alliance concluded with Pfizer Inc. in 2014 enabled us to jointly develop Bavencio® (avelumab). Following approvals for patients with metastatic Merkel cell carcinoma and those with locally advanced or metastatic urothelial carcinoma (UC) in 2017, the United States Food and Drug Administration (FDA) and the European Commission issued approvals for Bavencio® plus Inlyta® (axitinib) for the first-line treatment of patients with advanced renal cell carcinoma in 2019. Last year, the FDA approved Bavencio® for the maintenance treatment of patients with locally advanced or metastatic urothelial carcinoma that has not progressed with first-line platinum-containing chemotherapy. This year the European Commission (EC) and the Japanese Ministry of Health, Labour and Welfare (MHLW) approved Bavencio® as monotherapy for the first-line maintenance treatment of adult patients with locally advanced or metastatic urothelial carcinoma who are progression-free following platinum-based chemotherapy. Additional applications for Bavencio® have been submitted to regulatory authorities worldwide.

Mavenclad® (cladribine tablets) was approved by the European Commission in 2017. It is the first short-course oral treatment approved in Europe for the treatment of relapsing multiple sclerosis (RMS) in patients with high disease activity. With the approvals in a number of additional countries in 2018 and 2019, including the United States and Switzerland, Mavenclad® is now approved in more than 80 countries. This year, independent data has shown that Mavenclad®-treated patients receiving an mRNA Covid-19 vaccine mount a similar antibody response to that of the general population which is important since new strains of Covid-19 push the pandemic onward and guidance recommends booster vaccinations. New data presented at the European Committee for Treatment and Research in Multiple Sclerosis (ECTRIMS) 2021 highlight improvement in measures of physical and mental health of patients with relapsing multiple sclerosis after one year of treatment with Mavenclad®. Late-breaking real-world data suggest the sustained benefit of Mavenclad® treatment on long-term mobility and disability status.

The oncology drug Tepmetko® (tepotinib) was the first oral MET inhibitor to receive regulatory approval anywhere in the world for the treatment of advanced non-small cell lung cancer (NSCLC) harboring mesenchymal-epithelial transition (MET) gene alterations, with its approval in Japan in March 2020. In February, the FDA approved Tepmetko® for the treatment of patients with metastatic non-small cell lung cancer harboring MET exon 14 skipping alterations. Tepmetko® is the first and only FDA approved MET inhibitor that offers once-daily oral dosing. This indication is approved under accelerated approval based on overall response rate and duration of response. The continued approval may be contingent upon verification and description of clinical benefit in confirmatory trials. In December 2021, the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) adopted a positive opinion recommending the granting of a full marketing authorization for Tepmetko® as the first and only oral MET inhibitor for adult patients with advanced NSCLC harboring alterations leading to METex14 skipping. The CHMP positive opinion will now be reviewed by the European Commission, with a decision expected in the first quarter of 2022.

In addition to marketing already approved medicines, we are pushing ahead with research projects in other important therapeutic areas. The portfolio of projects is evaluated on a regular basis. This may also lead to in-licensing or out-licensing, or further strategic alliances.

The development of our Bruton’s tyrosine kinase (BTK) inhibitor Evobrutinib is further progressing. New data presented at the 37th Congress of the ECTRIMS show that Evobrutinib is the first BTK inhibitor to demonstrate a significant reduction in slowly expanding lesions (SEL) in patients with RMS. SELs are chronic, active,

demyelinated multiple sclerosis (MS) lesions, which are thought to be an early indicator of disease progression in MS. Additionally, the enrolment in the Phase III Evolution RMS clinical trial program has been completed. It is evaluating the efficacy and safety of investigational BTK inhibitor Evobrutinib in patients with relapsing multiple sclerosis. Evobrutinib is an oral, highly selective inhibitor BTK and a potential innovation for people living with MS, as it may offer a novel dual mechanism of action that is thought to impact myeloid cells in addition to B-cells and thus could address MS pathobiology in a fundamentally new way. The data from a Phase II placebo-controlled randomized trial showed that the BTK inhibitor Evobrutinib significantly reduced blood neurofilament light chain levels, a key biomarker of neuronal damage and inflammation, in patients with multiple sclerosis.

In March, we announced a worldwide in-licensing agreement with Debiopharm, Lausanne, Switzerland, for the development and commercialization of Xevinapant (Debio 1143). Xevinapant, a potent oral Inhibitor of Apoptosis Proteins (IAP) antagonist, is the only medicine in its class in late-stage clinical development and has the potential to be first-in-class. Xevinapant is currently being investigated in the Phase III TrilynX study for previously untreated high-risk locally advanced squamous cell carcinoma of the head and neck (LA SCCHN), in combination with platinum-based chemotherapy and standard fractionation intensity-modulated radiotherapy.

In April, we announced key clinical advancements for berzosertib (M6620), an investigational, potent and selective ataxia telangiectasia and Rad3-related (ATR) inhibitor. Berzosertib is the leading asset in our DNA damage response (DDR) inhibitor program and one of the most advanced ATR inhibitors in oncology clinical development industry-wide. We are leading more than ten clinical trials across DNA Damage Response (DDR) pathways in various tumor types.

In December, we announced the strategically focused expansion of our neurology pipeline with the acquisition of the rights to develop cladribine for the treatment of generalized myasthenia gravis (gMG) and neuromyelitis optica spectrum disorder (NMOSD). We entered into an agreement to secure the global rights by acquiring Chord Therapeutics, a Swiss-based biotech company focused on rare neuroinflammatory diseases. We expect the transaction to be closed in early 2022 after satisfactory completion of customary closing conditions.

With Enpatoran and M1231 we have two additional assets in our portfolio with first-in-class potential. M1231 is a MUC1/ EGFR bi-specific Antibody-Drug Conjugate (ADC) that has an enhanced safety profile compared to existing ADC therapies. We consider this asset as next generation ADC for patients with solid tumors aiming for effective delivery of potent chemotherapy payload with reduced on- and off-target toxicity. Enpatoran is a small molecule for targeted inhibition of the important lupus mediator TLR7/8, aiming for improved efficacy with low infection risk. For Enpatoran, we plan to initiate a Phase II study in CLE (Cutaneous lupus erythematosus) and SLE (Systemic Lupus Erythematosus) in early 2022.

Sometimes, development projects are discontinued after high levels of investment at a late phase of clinical development. Decisions – such as those relating to the transition to the next clinical phase – are taken with a view to minimizing risk. We are currently not aware of any risks beyond general development risks that could significantly affect the net assets, financial position, and results of operations.

Furthermore, there is the risk that regulatory authorities either do not grant or delay approval or grant only restricted approval. Additionally, there is the risk that undesirable side effects of a pharmaceutical product could remain undetected until after approval or registration, which could result in a restriction of approval or withdrawal from the market. Well-advanced programs in our pipeline and those of our partners result in potential new approvals; on the other hand, missing targets in this area may have substantial to critical effects on our financial position and operating result, for example due to lower net sales or the non-occurrence of milestone payments from collaboration agreements. These risks are evaluated with probabilities ranging from improbable to likely.

For more detailed description on our R&D activities worldwide, please refer to the section "**Research and Development**" in "**Fundamental Information about the Group**" in the annual report.

Opportunities presented by activities to boost innovative strength

Digital technologies and data are becoming increasingly important. They will enable the development of personalized solutions of the future, accelerate our R&D pipelines, and ultimately improve patient and customer outcomes. In this context, developing and adhering to rigorous ethical standards is of utmost importance for all our activities. Therefore, we created the Merck Digital Ethics Advisory Panel to provide external guidance and expertise on complex ethical matters around data usage, algorithms, and new digital innovations, ensuring that the company develops new digital technologies responsibly. In 2021, we established the Code of Digital Ethics, which serves as a basis for ethical risk assessment in existing ventures but is also utilized to design ethics checkpoints for nascent digital solutions throughout the company. To stay ahead of the curve, we are bringing innovation and digitalization closer together.

We look into transformative technologies and innovative (digital) business models beyond our core products and markets while keeping in strategic proximity to our business sectors. Examples for transformative technologies include our innovation fields Cultured Meat and Bioelectronics. We are cooperating with start-ups and companies in our and other industries to drive innovative approaches.

Opportunities provided by CRISPR technology

As a pioneer of genome-editing innovation for nearly two decades, we are leveraging CRISPR technology as a core competency of our business. Around the world, our Life Science business sector holds 40 CRISPR-related patents in methods and composition, including the fundamental technology of CRISPR Cas9 for gene editing and integration in mammalian cells and paired Cas9 nickases. Two of the CRISPR-Cas9-assisted genome-editing patents are available in the United States, allowing us to support US scientists and researchers in their work to advance and protect gene-therapy development programs. In the reporting year, we signed an agreement licensing our CRISPR-Cas9 technology to Cellecta, Inc., a functional genomics products and services provider based in Mountain View, California, United States. Through the licensing of our innovative technology, we are paving the path for researchers and scientists to identify and accelerate next-generation treatments.

Risks and opportunities related to the quality and availability of products

Opportunities arising from capacity expansion

In Life Science, we opened our second Carlsbad, California-based facility in the United States, significantly expanding our global contract development and manufacturing organization (CDMO) footprint. The new € 100 million, 140,000-square foot facility will more than double the company's existing capacity to support large-scale commercial and industrial manufacturing for viral gene therapy, in a market expected to grow to US$ 10 billion by 2026. This is the company's second Carlsbad, California-based facility to serve cell and gene therapy customers driven by the industry's rapid adoption of viral vector-based therapies. With the acquisition of Exelead and AmpTec we will further strengthen our CDMO offering for mRNA. Exelead specializes in complex injectable formulations, including Lipid Nanoparticle-based drug delivery technology which is key in mRNA therapeutics for use in Covid-19 and many other indications. AmpTec's PCR-based technology combined with our expertise in lipides manufacturing allows us to offer customers innovative technologies, products and services to help advance life-enhancing therapeutics and vaccines for Covid-19. Additionally, our Life Science business sector has been awarded a € 121 million contract award for the construction of a lateral flow membrane production facility over a three-year period at our U.S. site in Sheboygan, Wisconsin, United States. The contract award from the U.S. Department of Defense, on behalf of the U.S. Department of Health and Human Services, is part of an effort to ensure secure local supply and production capacity for critical products for pandemic preparedness. We further broadened our manufacturing footprint with a combined € 40 million investment at our production facilities in Danvers, Massachusetts, and Jaffrey, New Hampshire, United States. These sites supply critical products to customers developing lifesaving therapies, including Covid-19 vaccines, as well as provide products and services for biopharmaceutical manufacturing. These expansions will significantly increase capacity and output at these facilities by 2022, respectively, and create nearly 700 new manufacturing positions. Furthermore, we announced the addition of a single-use assembly production unit at

our site in Molsheim, France, the first site in Europe to produce this product critical to the manufacture of Covid-19 vaccines and other life-saving therapies.

In Electronics, we plan to invest more than € 3 billion in innovation and capacities up to the end of 2025. We will continue to heavily invest in research and development (R&D) in leading-edge material solutions and plan to spend more than € 2 billion in long-term fixed assets (capital expenditures). The investment is an essential part of the business sector's Level Up growth program, as announced at our Capital Markets Day on September 9. Through Level Up, Electronics seeks to capture the growth opportunities that come along with the significantly accelerating global demand for innovative semiconductor and display materials. This demand is driven by exponential data growth and highly impactful technology trends such as the Internet of Things and 5G. Level Up will initiate or accelerate important internal initiatives under the Capabilities priority. Among other things, it will further leverage its data analytics capabilities and invest even further into the safety realm.

Risk of a temporary ban on products/production facilities or of non-registration of products due to non-compliance with quality standards

We are required to comply with the highest standards of quality in the manufacturing of pharmaceutical products (Good Manufacturing Practice or official pharmacopoeia). In this regard, we are subject to the supervision of the regulatory authorities. Conditions imposed by national regulatory authorities could result in a temporary ban on products/production facilities, and possibly affect new registrations with the respective authority. We make the utmost effort to ensure compliance with regulations, regularly perform our own internal inspections, and carry out external audits. Thanks to these quality assurance processes, the occurrence of a risk with a substantial impact is improbable; however, it cannot be entirely ruled out. Depending on the product concerned and the severity of the objection, such a risk might have a negative impact on the net assets, financial position, and results of operations.

Risks of production availability

Further risks include operational failures due to fire or force majeure, for example natural disasters such as floods or earthquakes, which could lead to a substantial interruption or restriction of business activities. Insofar as it is possible and economically viable, the Group limits its damage risks with insurance coverage, the nature and extent of which is constantly adapted to current requirements. Likewise, we are exposed to risks of production outages and the related supply bottlenecks that can be triggered by technical problems in production facilities with very high-capacity utilization. Furthermore, there are risks of supply bottlenecks due to a lack or disappearance of capacity. We are working to continuously mitigate the risks by making regular investments, setting up alternative sourcing options, and maintaining inventory levels.

Although the occurrence of these risks is considered highly improbable, an individual event could have a critical negative effect on the net assets, financial position, and results of operations.

Risks of dependency on suppliers

In balanced markets, single-sourcing strategies may be chosen to bundle our company's demand and accelerate price reductions. This strategy might result in dependency on individual suppliers for a number of goods or services. Consequently, events like discontinued/curtailed production or supply disruptions could potentially result in unavailability of such goods or services and have a critical impact on the concerned businesses. The Covid-19 pandemic represented an additional force, driving the potential risks of the single-source strategies. With long-term strategic alliances, qualification and validation of alternative sources, and supplier development strategies, we are able to reduce the probability of occurrence of these risks and rate them as possible.

Product liability risks

Companies in the chemical and pharmaceutical industries are particularly exposed to product liability risks. Product liability risks can lead to considerable claims for damages, loss of reputation, and costs to avert damages. We have taken out the liability insurance that is standard in the industry for such risks. However, it could be that the insurance coverage available is insufficient for individual cases. Although the occurrence of product liability claims in excess of the existing insurance coverage is considered highly improbable, individual cases could still have a critical effect on the net assets, financial position, and results of operations.

Risks due to product-related crime

As a leading global science and technology company and manufacturer of products of the highest quality, we are exposed to various security- and crime-related risks. Due to the increasing complexity of global trade, our products are particularly at risk from counterfeiting, theft, illegal diversion, and misuse. If left unaddressed, this would not only lead to financial loss, reputational damage, and business disruption but also impact patient & customer safety. Consequently, we have implemented technical, operational, and procedural measures aimed at protecting the integrity of our products and supply chains, whilst also ensuring new threats are identified and addressed. Overall, the threat resulting from product-related crime is likely with a potential moderate impact.

Risks and opportunities from the use of social media

Merck and its employees are active on numerous social media channels. The consistent and legally compliant use of the channels and their content is important in terms of increasing awareness of our brand, among other things. Merck takes precautions and implements processes to ensure awareness of the proper handling of social media, controlling publication, and actively managing communication.

Nevertheless, reputational risks could result, for instance through public dialogues in social media. We thus rate this as a moderate risk.

Financial risks and opportunities

As a corporate group that operates internationally, and due to our presence in the capital market, we are exposed to various financial risks and opportunities. Above all, these are liquidity and counterparty risks, financial market risks and opportunities, risks of fluctuations in the market values of operational tangible and intangible assets, as well as risks and opportunities from pension obligations.

Risk and opportunity management in relation to the use of financial instruments

In the area of financial risks and opportunities, we use an active management strategy to reduce the effects of fluctuations in exchange and interest rates. The management of financial risks and opportunities by using derivatives is regulated by extensive guidelines. Speculation is prohibited. Derivative transactions are subject to constant risk controls. The strict separation of functions between trading, settlement, and control functions is ensured.

Liquidity risks

To ensure its continued existence, a company must be able to always fulfill its commitments from operating and financial activities. Therefore, to reduce potential liquidity risks, we have a central Group-wide liquidity management system in place, and a balanced maturity profile. The maturities of our financial liabilities are aligned with our planned free cash flow. Furthermore, we have a syndicated loan facility of € 2 billion with a term until 2025, which ensures continuing solvency if any liquidity bottlenecks occur. As our loan agreements do not contain any financial covenants, these agreed lines of credit can be accessed even if Merck's credit rating should deteriorate. Additionally, we have a commercial paper program with a maximum volume of € 2 billion.

Counterparty risks

Counterparty risks arise from the potential default by a partner in connection with financial investments, loans, and financing commitments on the one hand and receivables in operating business on the other.

As for counterparty risks from financial transactions, we review all central positions relating to trading partners and their credit ratings daily. We manage financial risks of default by diversifying our financial positions and through the related active management of our trading partners. Significant financial transactions involving credit risk are entered into with banks and industrial companies that have a good credit rating. Moreover, our large banking syndicate – the syndicated loan facility of € 2 billion was syndicated amongst 19 banks – reduces possible losses in the event of default.

The solvency and operational development of trading partners are regularly reviewed as part of the management of operational counterparty risks. Sovereign risks are also analyzed. The volume of receivables of each customer is capped in line with their credit ratings. Risk-mitigating measures, such as credit insurance, are utilized as appropriate. Nevertheless, defaults by isolated trading partners, even those with outstanding credit ratings, cannot be entirely ruled out, although rated as unlikely (further information can be found in "**Credit risks**" in the note "**Management of financial risks**" in the Notes to the Consolidated Financial Statements).

Counterparty risk is classified as a possible risk with a moderate effect.

Financial market risks and opportunities

As a result of our international business activities and global corporate structure, we are exposed to risks and opportunities from fluctuations in exchange rates. These result from financial transactions, operating receivables, and liabilities, as well as forecast future cash flows from sales and costs in foreign currency. We use derivatives to manage and reduce these risks and opportunities (further information can be found in the note "**Derivative financial instruments**" in the Notes to the Consolidated Financial Statements). Foreign exchange rate risks are rated as possible with a potential substantial effect on the net assets, financial position, and results of operations.

Variable interest and current financial liabilities are exposed to the risks and opportunities of interest rate fluctuations. These are also managed and reduced using derivatives. Interest rate risks have a potentially negative impact, are considered possible, and pose an immaterial risk overall.

Risks of impairment of balance sheet items

The carrying amounts of individual balance sheet items are subject to the risk of changing market and business conditions and thus to changes in fair values as well. Necessary impairments could have a significant negative non-cash impact on earnings and affect the accounting ratios. This applies in particular to the high level of intangible assets including goodwill, which mainly derive from the purchase price allocations made in connection with past acquisitions (further information can be found in the notes “**Goodwill**” and "**Other intangible assets**" in the Notes to the Consolidated Financial Statements). All relevant risks were assessed during the preparation of the Consolidated Financial Statements and were taken into account accordingly. We rate risks beyond this as improbable with a potential critical impact.

Risks and opportunities from pension obligations

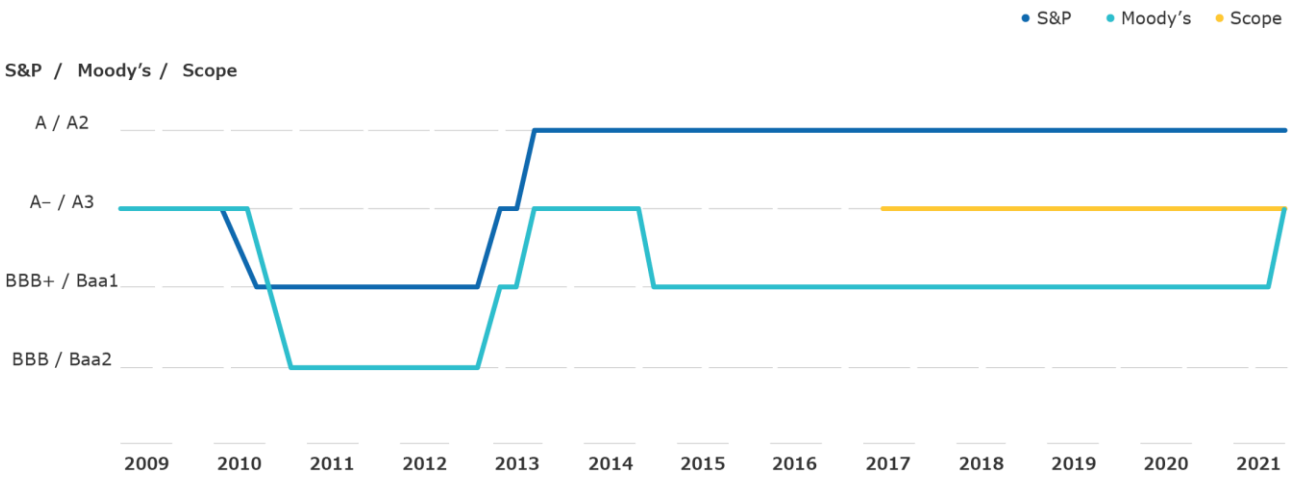
We have commitments in connection with pension obligations. The present value of defined benefit obligations can be significantly increased or reduced by changes in the relevant valuation parameters, for example the interest rate or future salary increases. Pension obligations are regularly assessed as part of annual actuarial reports. The obligations are covered by the pension provisions reported in the balance sheet based on the assumptions as of the balance sheet date. Some of these obligations are funded by plan assets (further information can be found in the note "Provisions for pensions and other post-employment benefits" in the Notes

to the Consolidated Financial Statements). To the extent that pension obligations are covered by plan assets consisting of interest-bearing securities, shares, real estate, and other financial assets, decreasing or negative returns on these assets can adversely affect the fair value of plan assets and thus result in further additions to pension provisions. By contrast, rising returns increase the value of plan assets, thereby resulting in excess cover of plan liabilities. We increase the opportunities of fluctuations in the market value of plan assets on the one hand and reduce the risks on the other by using a diversified investment strategy. The possible risk due to pension obligations could have minor effects on the net assets, financial position, and results of operations.

Assessment by independent rating agencies

The capital market uses the assessments published by rating agencies to help lenders assess the risks of a financial instrument used by Merck. We are currently rated by Standard & Poor's, Moody's, and Scope. Standard & Poor's has issued a long-term credit rating of A with a stable outlook, Moody's a rating of A3 with a stable outlook, and Scope a rating of A- with a positive outlook. In line with market procedures, our financing conditions are closely tied to our rating. The better the rating, the more favorably we can generally raise funds on the capital market or from banks.

Overview of Rating Development



Tax risks

Merck and its subsidiaries operate worldwide and are consequently subject to different national tax laws and regulations. National tax audits of Merck entities are conducted on an ongoing basis by the tax authorities of the countries in which Merck operates. Tax risks result in particular from changes in national tax laws and regulations, case law and interpretation by national tax authorities, as well as from significant transactions such as acquisitions, divestments and reorganizations.

Findings of the national audit authorities of the various countries may lead to higher tax expenses and payments and may also have an impact on the amount of tax receivables and liabilities and on deferred tax assets and liabilities.

The resulting tax risks are regularly and systematically reviewed by the tax function. Appropriate standards are in place to identify tax risks at an early stage, review and assess them and minimize them accordingly. Measures to reduce risks are coordinated by the tax department with the national companies. Risks in addition to those already considered in the balance sheet are classified as improbable to possible with potential moderate to substantial impact on the net asset, financial position, and results of operations.

For information on the accounting and measurement policies for income taxes, please refer to the section "**Income tax**" in "**Notes to the Consolidated Financial Statements**" in the annual report.

Legal risks

Generally, we strive to minimize and control our legal risks. To this end, we have taken the necessary precautions to identify threats and defend our rights where necessary.

Nevertheless, we are still exposed to risks from litigation or legal proceedings. In particular, these include risks in the areas of product liability, competition and antitrust law, pharmaceutical law, patent law, trademark law, data protection law, tax law, and environmental protection. As a research-based company, we have a valuable portfolio of industrial property rights, patents, and brands that could become the target of attacks and infringements. The outcome of future proceedings or those currently pending is difficult to foresee.

For instance, we are currently involved in litigation with Merck & Co. Inc., Kenilworth, NJ, United States (outside the United States and Canada: Merck Sharp & Dohme Corp. (MSD)), against whom we have filed lawsuits in various countries. This company has also sued us in the United States for trademark infringement, among other things.

Due to long statutes of limitations or in some cases the absence thereof, it is not possible to rule out that we will face third-party claims arising from the same issue despite the conclusion of legal proceedings. Court or official rulings or settlements can lead to expenses with a substantial to critical impact on our business and earnings.

Despite extensive precautionary measures, non-compliance with laws and regulations leading to related consequences can never be completely excluded.

In our opinion, the lawsuits described below constitute the most significant legal risks. This should not be seen as an exhaustive list of all legal disputes currently ongoing.

Risks due to antitrust and other government proceedings

Raptiva®: In December 2011, the federal state of São Paulo, Brazil, sued Merck for damages because of alleged collusion between various pharmaceutical companies and an association of patients suffering from psoriasis and vitiligo. This collusion is alleged to have been intended to increase sales of the medicines from the companies involved to the detriment of patients and state coffers. Moreover, patients are also suing for damages in connection with the product Raptiva®. Merck has taken appropriate accounting measures for these issues,

which relate to various legal cases. Risks in excess of this with a negative effect on the net assets, financial position, and results of operations cannot be ruled out, but are considered possible with minor impact.

Risks in connection with a settlement agreement concluded by the divested Generics group

Paroxetine: In the United Kingdom, Merck was subject to antitrust investigations by the British Competition and Market Authority (CMA) in connection with the generics business that was divested in 2007. In March 2013, the authorities informed Merck of the assumption that a settlement agreement entered into in 2002 between Generics (UK) Ltd., United Kingdom and several subsidiaries of GlaxoSmithKline plc, United Kingdom, in connection with the antidepressant drug paroxetine, violated British and European competition law. They stated that Merck was liable as the then-owner of Generics (UK) Ltd. And because it was involved in the negotiations for the settlement agreement. The investigations into Generics (UK) Ltd. started in 2011, without this being known to Merck. After the European Court of Justice confirmed in January 2020 that such settlement agreements can violate European competition law, the Competition Appeal Tribunal (CAT) set a low single-digit million euro figure fine in May 2021 that Merck paid in September of fiscal year 2021. The risk is considered to be more than likely with minor impact. A provision in a low double-digit million euro amount was recognized for the risk of additional potential claims as of December 31, 2021.

Citalopram: In connection with the generics business that was divested in 2007, Merck was accused of breaching EU antitrust law through agreements entered into by its former subsidiary Generics (UK) Ltd., relating to the antidepressant Citalopram patented by Lundbeck A/S, Denmark. The European Commission imposed a fine in June 2013. Merck filed a lawsuit against the Commission's decision with the European Court (EC) in August 2013. The lawsuit was rejected in 2016. Merck subsequently filed an appeal against this decision with the European Court of Justice (CJEU), which confirmed the first-instance ruling of the EC in March 2021. Although the fine of € 18 million was paid in 2013, additional potential claims were considered to be probable. A provision in a mid-double-digit million euro amount was recognized for these proceedings as of December 31, 2021. The risk is considered to be more than likely with minor impact.

Human resources risks

Our future growth is highly dependent on our innovative strength. Therefore, the expertise and engagement of employees in all sectors in which we operate are crucial to the success of the company. The markets relevant to the company are characterized by intensive competition for qualified specialists and talents, and by the challenge of being perceived by the public as an attractive employer. Fluctuation risks specific to countries and industries have to be identified ahead of time and specifically addressed in order to keep the skills and expertise critical to success and business within the company.

Recruiting and retaining specialists and talents are therefore key priorities for the company and are managed through the targeted use of, for instance, employer branding initiatives, global talent and succession management processes, as well as competitive compensation packages. Nevertheless, employee-related risks that affect business activities are possible, even though their impact is difficult to assess.

Information technology risks

We use a variety of IT systems and processes in order to optimally support our globalization. Trends in information technology offer various opportunities but also harbor risks.

Risks due to cybercrime and the failure of business-critical applications

Increasing international networking and the related possibility of IT system abuse are resulting in cybercrime risks for Merck, such as the failure of central IT systems, the loss of the data integrity or the disclosure of confidential data from research and business activities, the manipulation of IT systems in process control, or an increased burden or adverse impact on IT systems as a result of virus attacks.

The Merck Group operates an information protection management system based on ISO 27001, comprising security guidelines as well as organizational and technical measures to prevent and address IT security incidents. Globally used IT applications form the basis for the contractual delivery of products and solutions. The failure of business-critical IT applications could therefore have a direct influence on our ability to deliver and on the quality of our products. This also applies to the failure of a data center. To achieve the required service quality, we use a quality management system certified to ISO 9001 that also applies to the provision of IT. In addition, to reduce the risk of failure, we operate several redundantly designed data centers. Furthermore, insurance solutions for cybercrime offenses are in place at Group level.

Likewise, complications with the changeover of IT systems could negatively impact the earnings situation. Close monitoring of critical IT projects serves to mitigate this risk.

Despite the mitigating measures taken and functional continuity plans, the effects of cybercrime or the failure of business-critical IT applications and their influence on the net assets, financial position, and results of operations are considered to be possible and with potentially substantial impact.

Environmental, climate-related, and safety risks and opportunities

Risks arising from environment, climate as well as plant and equipment

As a company with global production operations, we are exposed to risks of possible damage to people, goods, and our reputation. Those include physical risks stemming from exposure to droughts, storms, and floods. Audits, consulting, and training on environmental protection and occupational health and safety minimize these risks to people and the environment. In order to ensure the continuity of plant and equipment, we monitor these risks both at our own sites as well as at suppliers and contract manufacturers. By adhering to high technical standards, our rules of conduct, and all legal requirements in environmental protection and occupational health and safety, we ensure the preservation of goods and assets. We have taken sufficient appropriate accounting measures for the environmental risks known to us. We monitor regulatory risks in connection with the transition to a low-carbon economy, which could materialize in the mid- and long-term through rising carbon prices through emissions trading systems, taxes or energy legislation. We mitigate those risks with our energy and carbon management measures. We classify these as possible risks based on which a substantial impact on the financial position cannot be ruled out.

Opportunities arising from the further integration of Sustainability in the Corporate Strategy

In 2020, we integrated sustainability more strongly in the corporate strategy, setting three goals in the areas of science and technology, value chain, and climate and environment. By considering the goals of the sustainability strategy when making business decisions, we contribute to achieving the United Nations Sustainable Development Goals. In 2021, we established the new Group Function “Corporate Sustainability, Quality and Trade Compliance”. Our dedication to sustainability paired with our commitment to quality, regulatory excellence, and compliance are important focus areas for us. Combining these strategic elements will ensure an effective and efficient execution of our strategy and enable us to cater to the increasing expectations of customers, patients, employees, investors, and the general public. Furthermore, we are promoting visionary sustainability projects in areas like the circular economy and digital sustainability.

Risks due to the divestment, acquisition, and integration of companies and businesses

Successfully acquiring and subsequently integrating new businesses entails risks. These are primarily centered around the uncertainty of reaching business targets and synergy goals, as well as staying within the planned integration budget. Divestments, on the other hand, could lead to liabilities and additional expenses related to potential indemnifications and commitments guaranteed in the sale transaction. Merck leverages on its solid acquisition track record to reduce the probability of any transaction-associated risks, by integrating lessons learned from past transactions, strong due diligence, and closely managed integration processes. Given the current situation, there are no major risks.

Overall view of the risk and opportunity situation and management assessment

The most significant individual risks in the businesses have been named in the report above, with business- and market-related risks being the most significant alongside IT and legal risks. Most notably, the ongoing Covid-19 pandemic increases existing risks related to more restrictive regulatory requirements regarding drug pricing and reimbursement, the demand for our products, business interruptions at our production facilities, lack of availability of good quality materials or services, risks related to research and development, and negative macroeconomic developments.

Following the concentrated risk mitigation measures taken – such as the implementation of management action (organizational responsibility and process improvements), existing insurance coverage, and accounting precautions – we were able to take counteraction, in particular against significant individual risks.

The overall risk of the Group, which is derived from the probability-weighted aggregation of the identified risks, leads to the assessment that an existence-threatening risk-scenario, for which coverage and financing of the losses are questionable, is highly improbable. We are convinced that we will also successfully manage the challenges described in the future, also benefiting from diversification through our different products and markets.

In our view, business-related opportunities offer the greatest potential. The activities listed hold significant opportunities for us in the medium to long term, beyond the underlying forecast period. We pursue the opportunities that arise and specify their expected effects in the forecast development of net sales, EBITDA pre, and operating cash flow. Furthermore, we will actively seek new opportunities, examine their implementation, and drive them forward where appropriate. If opportunities arise in addition to the forecast developments, or these occur more quickly than anticipated, this could have positive effects on our net assets, financial position, and results of operations.