Fundamental Information about the Group

The Group

We are a vibrant science and technology company. Science is at the heart of everything we do. It drives the discoveries we make and the technologies we create. We make a positive difference in the lives of millions of people every day.

The digital platform and the products and services in our Life Science business sector make precision research simpler and help speed up scientific breakthroughs. They enable quicker access to healthcare and ensure that analyses are accurate and medications are trustworthy. In the Healthcare business sector, we accompany people in every phase of their life and help them to shape, improve, and prolong it. We enable personalized treatments for serious illnesses and help many couples to realize their wish to have children. In our Electronics business sector, we are the company behind the companies, advancing digital living and changing the way we process information and make it available. Our innovations release the potential of data and open up possibilities for positively influencing the way we live.

Everything we do is fueled by a belief in science and technology as a force for good. It is a belief that has driven our work since 1668, and will continue to inspire us to find more joyful and sustainable ways to live, because we are curious minds dedicated to human progress.

Merck KGaA, Darmstadt, Germany, holds the global rights to the company name and brand. The only exceptions are Canada and the United States. In these countries, we operate as EMD Serono in the healthcare business, as MilliporeSigma in the life science business, and as EMD Electronics in the electronics business.

Apart from our three business sectors, our financial reporting presents five regions: Europe, North America, Asia-Pacific, Latin America, and the Middle East and Africa. As of December 31, 2021, we had 60,348 employees worldwide¹. The figure as of December 31, 2020 was 58,127 employees.

Important developments at Group level

Peter Guenter was appointed to our Executive Board effective January 1, 2021. He is responsible for the Healthcare business sector.

The Performance Materials business sector was renamed Electronics effective March 4, 2021. The new name is the visible result of the strategic realignment conducted over the past several years and underscores the current role of the business sector as one of the leading solutions providers on the electronics market.

Matthias Heinzel was appointed to our Executive Board effective April 1, 2021. He is responsible for the Life Science business sector.

Belén Garijo took over from Stefan Oschmann as Chair of the Executive Board effective May 1, 2021.

Our response to Covid-19*

As a science and technology company, we are convinced that we can help combat the global challenges resulting from Covid-19. Our top priority is ensuring the health and safety of our employees and their families and continuing our business activities for the benefit of the many patients, scientists, and customers who depend on us.

We continued to engage in combating Covid-19 in 2021, including accelerating the supply of urgently needed lipids as part of our strategic partnership with BioNTech and comprehensively expanding our production capacities for technologies and solutions that are required for the manufacture of Covid-19 vaccines and treatments.

To date, our products and services have supported more than 80 vaccine developers, more than 35 solutions for testing, and more than 50 monoclonal antibodies, plasma products, and antiviral drugs.

For more information on how we are contributing to address the global challenges posed by Covid-19, see the following sections on our Life Science and Healthcare business sectors. We have also compiled a detailed overview on our website: https://www.emdgroup.com/en/company/press/press-kits/corona-pandemic.html.

Life Science

We are a leading, global supplier of tools, research-grade chemicals, and equipment for academic labs, biotech and biopharmaceutical manufacturers, and the industrial sector. Together with our customers, our purpose is to positively impact life and health with science. With a strong focus on innovation, we are committed to delivering the products, services, and digital platforms to create a sustainable future for generations to come.

Across our Research Solutions, Process Solutions, and Applied Solutions business units, we collaborate with the global scientific community to deliver breakthrough innovations along with a broad and deep portfolio of more than 300,000 products.

Research Solutions provides customer solutions to scientists in academic institutions, government labs, research hospitals, pharmaceutical, R&D, and biotech organizations, empowering their efforts to accelerate science.

Process Solutions provides biopharmaceutical manufacturers with process development expertise and technologies, supporting them to develop and manufacture drugs safely, effectively, and cost efficiently. Our biopharmaceutical customers look for expertise and products to improve every step of their manufacturing process, while biotech startups look for holistic support to build and scale up their manufacturing. With approximately 25,000 products and services – including single-use manufacturing, filtration, chromatography and purification, virus reduction, pharma and biopharma raw materials, drug delivery compounds, and engineering and validation services.

In Applied Solutions, we aim to improve health across many areas of daily life with diagnostic solutions to ensure the safety of vaccines and other life-saving therapies as well as provide testing services to identify contaminants in food, air and water. We supply products and workflow solutions that streamline processes, lower costs and deliver consistent, reliable results for diagnostic, testing and industrial customers, with 62,000-plus products and services that include lab water instruments for water purification, consumables and services, microbiology and bio-monitoring, test assays, analytical reagents, and flow cytometry kits and instruments.

In 2021, Life Science generated 46 percent of Group sales as well as 50 percent of EBITDA pre (excluding Corporate and Other).

Our Response to Covid-19*

We are helping to respond to the Covid-19 pandemic with products and solutions that empower scientists to detect and characterize viruses and to develop and manufacture vaccines and therapies. We are committed to providing the necessary research tools and reagents, manufacturing processes and production products to aid the global scientific fight against this novel virus. We continue to support many of our customers working on Covid-19 projects through our products and services, providing for more than 35 testing solutions across RT-PCR, antigen, and antibody diagnostics for both high-throughput centralized and distributed point-of-care settings; more than 80 different vaccine programs, consisting of several platforms that include DNA, Inactivated, Live Attenuated Virus, Viral Vector, Protein Subunit and mRNA; and more than 50 monoclonal antibodies, plasma-derived products and antiviral treatments. Additionally, through our eCommerce platform, <u>www.sigmaaldrich.com</u>, we provide a one-stop shop of more than 200 of the most commonly-used products and corresponding information for academic labs and biopharmaceutical companies working on Covid-19 diagnostic tests, vaccines and treatments.

We have also tapped into existing collaborations to support projects that target Covid-19 vaccine and therapy development. We have extended our partnership with BioNTech, for which we supplied key materials for their manufacturing platforms with a focus on therapies for cancer; today, we supply lipids for the drug delivery of BioNTech's mRNA-based Covid-19 vaccine, which is now approved for use in many countries.

As the pandemic continues, a global task force actively evaluates the overall supply chain of both products and key raw materials suppliers to mitigate any potential disruption. Leveraging business continuity plans, we remain dedicated to serving our customers in all markets. Protocols and guidelines have been set to minimize the impact to supply. Our 52 manufacturing sites and more than 100 distribution centers around the world remain operational to ensure that customers have the products and services they need to support the health of a global population.

Throughout all of this, we follow guidance outlined by the WHO, CDC and governments of impacted countries, and our global sites have relevant and approved preparedness plans and are empowered to act per their local scenarios, as necessary.

Research Solutions*

In 2021, we continued to collaborate with customers around the world to advance scientific progress.

Mid-year, we launched our new e-commerce platform with a simplified learning and buying journey on <u>www.sigmaaldrich.com</u>. The site was built to support an optimized experience for more flexible digital access. We introduced customers to an updated look and feel, enhanced mobile capabilities, 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 <u>www.sigmaaldrich.com</u> 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. In 2021, we supported more than 26 million global users in over 77 million sessions, with total e-commerce sales growing 22.4% over the previous year, totaling more than ≤ 1.45 billion.

Process Solutions*

A key goal for our Life Science business sector is to support our customers that manufacture drugs, from small to large innovator companies, bring safe and effective life-enhancing therapies and vaccines to millions of patients around the world. To that end, we continued to leverage strategic opportunities to enhance our capabilities and expand our products and services offering.

In January, we announced the acquisition of AmpTec GmbH, a leading Hamburg, Germany-based, mRNA contract development and manufacturing organization, to strengthen our capabilities to develop and manufacture mRNA for customer use in vaccines, treatments and diagnostics applicable in Covid-19 and many other diseases.

In February, we announced the further expansion of our strategic partnership with BioNTech SE, Mainz, to accelerate supply of urgently-need lipids used for the production of the Pfizer-BioNTech vaccine (BNT162b2).

Also, in February, we also announced an agreement with Alteogen, Inc., of South Korea, to provide latestage Contract Development and Manufacturing organization (CDMO) services through our BioReliance[®] End-to-End Solutions to develop and produce recombinant biologics used in the development and clinical evaluation of next-generation therapeutics from monoclonal antibody drugs.

In May, we launched a new, high-purity synthetic cholesterol product to meet the high demand for lipids, a key component of mRNA-based vaccines and therapeutics. Under the SAFC[®] brand of products, this launch occurred nine months ahead of schedule and increases capacity by the factor 50. We are one of a few companies that produces lipids in quantities needed to meet demand for mRNA therapeutics, including the Pfizer-BioNTech Covid-19 vaccine.

In October, we launched two new technologies to advance antibody-dug conjugates (ADC) therapies. These initiatives underscore our continued investment in novel modalities and support our efforts to double our ADC and high-potent active pharmaceutical ingredient (HPAPI) capacity in the near future. With the launch of the ChetoSensar[™] technology, we are working to address the hydrophobicity of ADCs. The new Dolcore[™] platform significantly reduces the development and time required to manufacture ADCs, increasing speed-to-market for a novel Dolostatin-based ADC payload by up to a year.

Applied Solutions*

In January, we launched the new Milli-Q[®] EQ 7000 Type 1 water purification system to expand our benchtop ultrapure water system portfolio. The new Milli-Q[®] EQ 7000 system produces consistent ultrapure water quality that is easily customized to experimental requirements, strengthening our Milli-Q[®] ultrapure water offering.

In December, the U.S. government awarded a € 121 million contract for the construction of a lateral flow membrane production facility, over a three-year period, at our site in Sheboygan, Wisconsin, United States. The contract, received 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.

Investments to expand capabilities and production^{*}

In March, we announced the acceleration of our European expansion plans by adding a single-use assembly production unit at our site in Molsheim, France. With the \in 25 million investment, we are responding to the unprecedented global demand of this key technology, which is used for the production of Covid-19 vaccines and other lifesaving therapies.

In June, we announced an investment to strengthen our development and production of monoclonal antibodies and other life-saving medicines and vaccines. This includes € 50 million to strengthen bioproduction activities at our site in Martillac, France, involving the creation of 150 jobs until 2024. Combined with our investment in Molsheim, France, these expansion plans are part of an ambitious multi-year program aimed at expanding the industrial capacities of our business sector to meet growing global demand for life-saving drugs and make a significant contribution to global public health.

In October, we announced the opening of our second Carlsbad, California, United States-based facility, significantly expanding our global Contract Development Manufacturing Organization (CDMO) footprint. This new \in 100 million, 13,000 square meter facility will more than double our existing capacity to support large-scale commercial and industrial manufacturing for viral gene therapy, in a market expected to grow to \notin 9 billion by 2026.

Healthcare

Healthcare discovers, develops, manufactures, and markets innovative pharmaceutical and biological prescription drugs to treat cancer, Multiple Sclerosis (MS), infertility, growth disorders, and certain cardiovascular and metabolic diseases. Healthcare operates across four therapeutic areas: Neurology and Immunology, Oncology, Fertility, and Cardiology Metabolism & Endocrinology with a clear ambition to become a global specialty innovator. Our R&D pipeline positions us with a clear focus on strengthening our leadership positions in oncology, neurology, and immunology.

Since the start of the Covid-19 pandemic, we have been continuously making every effort to proactively handle the situation and minimize the impact of the pandemic on the supply of our medicines locally and globally through three main levers: the thorough implementation of our business continuity plans across our network, the active management of our stocks, and the assessment of alternative transportation routes to reach our customers and patients.

In 2021, Healthcare generated 36% of Group sales and 33% of EBITDA pre (excluding Corporate and Other). Europe and North America generated 55% of Healthcare's net sales in 2021. In recent years, we have steadily expanded our presence in growth markets. In 2021, Asia-Pacific and Latin America accounted for 38% of sales.

Neurology & Immunology*

We have a long-standing legacy in neurology and immunology including more than two decades of experience in Multiple Sclerosis (MS), and are committed to people living with neuroinflammatory and immune-mediated diseases by focusing on finding solutions addressing unmet medical needs. Our current MS portfolio includes two approved products for the treatment of relapsing MS (RMS) – Rebif[®] (interferon beta-1a) and Mavenclad[®] (cladribine tablets). In addition, we have our investigational MS treatment evobrutinib, which is the first Bruton's tyrosine kinase (BTK) inhibitor to complete Phase III trial enrollment.

In March of this year, French Health Authorities approved Mavenclad[®] and made it available and reimbursed for people living with MS in France. With this, Mavenclad[®] is now approved in more than 80 countries worldwide, including those of the European Union, Switzerland, Australia, Canada and the United States. We view

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Mavenclad[®] as a complementary oral treatment option in our MS product portfolio. Rebif[®], a disease-modifying drug used to treat RMS, is and remains a well-established therapy. Rebif[®] has been a standard treatment in RMS for more than 20 years and has more than 1.6 million patient-years of therapy since approval.

Generating data around our MS treatments and the risk of respiratory viral infections has remained important also this year, helping to support clinicians as they make treatment decisions for their patients living with MS. In February, we presented new data from the MAGNIFY-MS study at the Americas Committee for Treatment and Research in Multiple Sclerosis (ACTRIMS) Forum 2021 (for further details see "Research & Development").

Further data relevant for treatment during Covid-19 were presented at the 2021 American Academy of Neurology (AAN) Annual Meeting in April (for further details see "Research & Development").

In May, we announced the completion of an out-licensing agreement with MoonLake Immunotherapeutics AG for sonelokimab (M1095) (for further details see "<u>Research & Development</u>").

We presented a total of 39 abstracts at the 37th Congress of the European Committee for Treatment and Research in Multiple Sclerosis (ECTRIMS) in October (for further details see "Research & Development").

New evobrutinib data were also presented at ECTRIMS, showing that evobrutinib was effective reducing the volume of slowly expanding lesions (SEL), an imaging biomarker of chronic active inflammation and axonal loss within the central nervous system (CNS), making it the first BTK inhibitor to show a significant effect on this biomarker (for further details see "Research & Development").

In December we announced a strategically focused expansion of our neuroinflammatory pipeline with the acquisition of the rights to develop cladribine for the treatment of generalized myasthenia gravis (gMG) and neuromyelitis optica spectrum disorder (NMOSD).

Oncology*

Erbitux[®] (cetuximab) is the best-selling drug in terms of revenue in the portfolio of our Biopharma business and is our flagship product in oncology. Treating more than 1 million patients since authorization, the product is a standard of care for patients with epidermal growth factor receptor (EGFR)-expressing, RAS wildtype metastatic colorectal cancer (mCRC), as well as both recurrent and/or metastatic and locally advanced squamous cell carcinoma of the head and neck (SCCHN).

Together with Pfizer Inc., we have made progress in sharing new data, obtaining additional regulatory approvals and reimbursement decisions with our anti-PD-L1 antibody Bavencio[®] (avelumab) (for further details see "Research & Development").

On January 25, the European Commission approved Bavencio[®] monotherapy for the first-line maintenance treatment of adult patients with locally advanced or metastatic urothelial carcinoma (UC) who are progression-free following platinum-based chemotherapy. This follows the approval of Bavencio[®] for this indication by the US Food and Drug Administration (FDA) in June 2020. Bavencio[®] is now approved as a first-line maintenance treatment for advanced UC in 39 countries and has become a standard of care in the treatment of this disease, based on the results of the JAVELIN Bladder 100 trial, the only Phase III study of an immunotherapy to demonstrate a significant overall survival benefit in the first-line setting.

Other highlights from our development pipeline included the advancement of several potential first-inclass/best-in-class compounds. The development program for tepotinib, our oral MET inhibitor designed to inhibit the oncogenic MET receptor signaling caused by *MET* (gene) alterations, has continued to achieve several milestones in 2021. Discovered in-house at our company, tepotinib underscores our strategic focus on delivering innovative precision medicines to patients with cancer.

On February 3, tepotinib was approved by the US Food and Drug Administration (FDA) with the brand name Tepmetko[®] (tepotinib) following Priority Review for the treatment of adult patients with metastatic non-small cell lung cancer (NSCLC) harboring mesenchymal-epithelial transition (MET) exon 14 skipping alterations. Tepmetko[®] is the first and only FDA approved MET inhibitor that offers once-daily oral dosing and is administered as two 225 mg tablets (450 mg). This indication was approved under accelerated approval based on overall response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials. In December 2021, Tepmetko became the first and only oral MET inhibitor to receive the Committee for Medicinal Products for Human Use (CHMP) positive opinion in Europe for adult patients with advanced NSCLC harboring alterations leading to METex14 skipping. Tepotinib is available in a number of other countries, and under review by various other regulatory authorities globally.

On September 30, we announced a mutual decision to end the global strategic alliance with GSK to develop bintrafusp alfa, the investigational bifunctional fusion protein designed to simultaneously block TGF- β and PD-L1. This decision was based on the clinical trial data generated to date, including three randomized clinical trials that did not demonstrate a benefit to patients. Based on these findings, several remaining studies in the program were also discontinued, including those in non-small cell lung cancer, triple negative breast cancer, biliary tract cancer, and bladder cancer. Based on the data generated during the agreement, no milestone payments were made by GSK and no future milestone obligations remain (for further details see "Research & Development").

Our broad portfolio of small-molecule DNA Damage Response (DDR) inhibitors represents multiple development paths as monotherapies or in combination with immunotherapy, chemotherapy or radiotherapy On April 12, we announced initiation of a Phase II trial with registrational intent for berzosertib, the leading asset in our DNA damage response (DDR) inhibitor development program, to further assess berzosertib in combination with topotecan for the treatment of relapsed, platinum-resistant small cell lung cancer (SCLC) (DDRiver SCLC 250). The berzosertib clinical development program is one of the most advanced Ataxia telangiectasia and rad3-related (ATR) inhibitor development programs industry-wide (for further details see "Research & Development"). Berzosertib, formerly known as VX-970, was licensed from Vertex Pharmaceuticals in 2017.

To augment the in-house innovations in our oncology portfolio with potential new solutions for patients with cancer, we entered a worldwide in-licensing agreement with Debiopharm, Lausanne, Switzerland, for the worldwide development and commercialization of xevinapant (Debio 1143), announced in March 2021. Xevinapant, a potent oral antagonist of Inhibitor of Apoptosis Proteins (IAP), 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. A second global Phase III study will be initiated in the first half of 2022 to evaluate xevinapant in patients with cisplatin-ineligible LA SCCHN.

Fertility*

As the global market leader in fertility drugs and treatments, our fertility franchise is an important growth driver for our Biopharma business. To date, over 4 million babies have been born with the help of GONAL- $f^{\otimes 2}$, a leading therapeutic within our fertility portfolio.

Infertility continues to represent an increasing challenge globally due to demographic changes and ongoing lifestyle adjustments like delayed childbearing. Despite the challenges we and our customers faced as a result of the Covid-19 pandemic, there was positive progress across our fertility portfolio in 2021 from launches to congress presentations and data studies. Overall, our fertility business has bounced back, making an exceptional contribution to the overall performance of our Healthcare business in 2021.

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¹ Chua, SJ, et al. Reprod Biol Endocrinol. 2021;19(1):1-13

During the Covid-19 pandemic, we further supported patients with advancing their treatment at home with the release of our Gonal-f[®] (follitropin alfa) 150 IU pen. In 2021, it was launched in Portugal, Finland and Poland, and we expect the first regulatory approvals in the APAC (Asia Pacific) region soon. A series of studies conducted with fertility patients and nurses highlighted both the ease of use and the patient-friendliness of our Gonal-f[®] pen.

Our Pergoveris[®] pen is the first product with a combination of recombinant follicle-stimulating hormone (r-hFSH) and recombinant luteinizing hormone (r-hLH) in a ready-to-use liquid version, eliminating the need for mixing. This makes it a suitable treatment option for women with severe FSH and LH deficiency. In Q3 2021, the Pergoveris[®] Pen was successfully launched in India, Mexico and Ecuador and is now available in 44 countries. Launches around the globe will continue in order to provide patients with access to this therapeutic.

Cardiology Metabolism & Endocrinology (CM&E)*

Every day, more than 90 million patients around the world use our trusted Cardiology Metabolism & Endocrinology (CM&E) medications. Concor[®], Euthyrox[®], Glucophage[®], and Saizen[®] are highly valued brands and market leaders in many key markets worldwide. As a result, CM&E is the largest business franchise of the Healthcare business sector in terms of sales, with strong growth in all major therapeutic areas of focus, contributing significantly to our overall profitability. Although no longer patent-protected, the brand equity of our products, built up over decades, makes them cornerstones for the treatment of chronic cardiovascular, metabolic, and endocrine diseases.

Concor[®]/Concor Cor[®], containing bisoprolol, is the leading beta-blocker worldwide in volume shares for treating hypertension and cardiovascular diseases such as coronary heart diseases and chronic heart failure. In addition to the plain preparations, the Concor[®] family offers fixed-dose combinations such as Concor Plus[®]/Lodoz[®] (bisoprolol with hydrochlorothiazide) and Concor AM[®] (bisoprolol with amlodipine).

Euthyrox[®], with the active ingredient levothyroxine, is the worldwide market leader for the treatment of hypothyroidism, a disease with high prevalence but still low diagnosis rates in most emerging markets.

Glucophage[®], containing the active ingredient metformin, is the drug of choice for first-line treatment of type 2 diabetes available in more than 100 countries. During 2021, multiple health authorities worldwide continued to approve Glucophage[®] in prediabetes when intensive lifestyle changes have failed. This indication for Glucophage[®] is now registered in 89 countries. Overall, considering the high prevalence of prediabetes and diabetes, we continue seeing great potential for Glucophage[®].

Saizen[®], with its active ingredient somatropin, is our main endocrinology product and is indicated for the treatment of growth hormone deficiency in children and adults. Saizen[®] can be delivered with the Easypod[®] electromechanical injection device, the only growth hormone injection device able to wirelessly transfer data such as injection times, dates, and doses to the web-based software system Easypod[®] Connect, making it easier for healthcare practitioners and patients to manage adherence and helping to reach their treatment goals. Aluetta[®] (the new Saizen[®] pen) is now available in 28 countries with the objective of expanding the reach of Saizen[®], offering additional options for healthcare practitioners and patients and expanding our devices portfolio.

In endocrinology, we differentiate ourselves from competitors through leadership in the eHealth space, both by building evidence and by leveraging the meaningful use of technology to provide new solutions for patient engagement, partnership with healthcare practitioners and better payer value proposition.

Electronics

We are the company behind the companies, advancing digital living. Our primary focus is on the electronics market with our materials and solutions changing the way we generate, access, store, process, and display information. In addition, our highly specialized, application-driven Surface Solutions business makes life more colorful. The business sector consists of three business units: Semiconductor Solutions, Display Solutions, and Surface Solutions. Comparing Electronics with a smartphone, Display Solutions represents the user interface, Semiconductor Solutions the intelligence, and Surface Solutions the aesthetics. We offer innovative solutions especially for the electronics industry – for microchips and displays – and for surfaces of every kind.

As part of our transformation program Bright Future, we repositioned ourselves and developed into a leading player in the global electronic materials market. At our Capital Markets Day on September 9, we announced the successful conclusion of our five-year Bright Future transformation, originally scheduled to take five years, two years ahead of schedule and introduced our new growth program Level Up. We seek to capture the growth opportunities that come 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. As a result, we upgraded our top-line guidance for the second consecutive time since the launch of Bright Future. As we shift from transformation into an execution and growth phase, we are aiming for an organic compound annual growth rate of 3% to 6% between 2021 and 2025.

On September 20, we announced our plans to invest significantly more than \in 3 billion in innovation and capacities until the end of 2025. These investments are an essential part of the new Level Up growth program. Within the scope of the program, we are addressing four mutually reinforcing key priorities: Scale, Technology, Portfolio, and Capabilities. We are investing in digital business models and data analysis competencies, as well as expanding our production and innovation capacities and footprints in close proximity to our customers. In addition, we will continue to evaluate external growth options, made possible by potential targeted bolt-on acquisitions. We will also invest further in our people and the capabilities required to enable the future growth trajectory.

Electronics accounted for 18% of Group sales in 2021, and its share of EBITDA pre (excluding Corporate and Other) was 17%. The EBITDA pre margin was 31.3% of net sales.

Semiconductor Solutions*

Semiconductor Solutions is at the heart of Electronics and is enabling the digital transformation in communications, mobility, and healthcare. As almost every electronic device uses one of our products, we are advancing virtually every aspect of digital living. We are developing solutions for smaller, faster, and more powerful devices. Semiconductor Solutions is the largest business unit in terms of sales within Electronics and offers materials, delivery systems, and services for the semiconductor industry. The overall semiconductor market is seeing strong growth with the rising adoption of digital technologies driven by recovering automotive markets and increasing smartphone demand amid wider availability of 5G networks.

The Semiconductor Materials business supplies products for every major production step in wafer processing, including doping, patterning, deposition, planarization, etching, and cleaning. Specialty cleans, photoresists, and conductive pastes for semiconductor packaging round off the portfolio. Our business fields are Thin-Film Solutions, Specialty Gases, Planarization, and Patterning Solutions. Intermolecular is our center for complex material solutions in Electronics, located in San Jose, California, USA. There, we explore, test, and develop combinations of advanced materials for next-generation electronics. Compared to conventional methods, our

approach provides significant time savings in the material development process, faster learning cycles, and detailed findings on new material combinations to provide a unique service for customers.

The Delivery Systems & Services business develops and deploys reliable delivery equipment to ensure the safe and responsible handling of gases and liquid materials with the highest quality and safety standards for electronic manufacturers.

Display Solutions*

Our Display Solutions business unit includes the businesses Liquid Crystals (LC), Organic Light-Emitting Diodes (OLED), Photoresists, Smart Antenna and Liquid Crystal Glazing. We support our display customers in developing novel display technologies and product concepts for applications, while also addressing new requirements that have emerged from the Covid-19 pandemic. With the proliferation of multiple applications and display trends, the display industry's technological requirements are significantly expanding. We are in a leading position to develop required new display materials and technology concepts to contribute to the diverse display landscape. We are active in the development of a broad range of display materials, including LCs, OLED, Quantum Dots Pixel Color Converters, and Display Patterning Materials (DPM).

In Liquid Crystals, we continue to see very dynamic market developments. Covid-19 has accelerated the market shift towards China and increased competition. We maintained our position as the technology leader with our XtraBright[™] products, winning new projects for large-area displays as well as high-resolution mobile devices. Our OLED and photoresist materials are used in multiple free-form display products. Our low-temperature processable positive tone photoresists are widely used to pattern on-cell touch sensors. These sensors enable a thinner display structure, which is crucial for foldable devices. Our Liquid Crystal Glazing business is receiving an increasing number of commercial orders for eyrise[®] i350 invisible privacy glazing. The transparent dynamic liquid crystal glass partitions can be switched on demand to create private spaces in public and commercial venues. In October, AVUS (automobile traffic and training road) in Berlin, Germany, celebrated the reopening of its main building which now displays a full eyrise[®] s350 Solar Shading facade. In September, we presented our Smart Antenna technology together with our development partners ALCAN Systems and NexTenna at SATELLITE 2021, the largest tradeshow in the satellite industry. Our LC-based technology licriOn[™] enables extensive connectivity access, even in remote areas where fast internet connections are unavailable or unaffordable today.

Surface Solutions*

The core markets for Surface Solutions are automotive coatings, cosmetics, and, to a smaller extent, industrial applications. We are serving these markets with functional and decorative solutions. Our main focus is on proactive solution development in close cooperation with our customers as well as expanding our portfolio through innovation in all areas. We provide our customers with solutions that help them to create innovative surfaces of all kinds. Our materials enable more beautiful, more resistant, and more effective product designs. Our pearlescent pigments allow striking automotive coatings, fascinating cosmetics, extraordinary packaging, and innovative product design. With a broad portfolio of active ingredients, we enable cosmetics manufacturers to enrich their skin care products with moisturizing, protecting, and anti-aging effects. Moreover, with our functional solutions we serve a large number of innovative applications, from dirt-repellent and easy-care surfaces to laser markings of plastic parts and cables.

Strategy*

Strategy fundamentals

We are curious minds dedicated to human progress. We believe that scientific exploration and responsible entrepreneurship are key to technological advances that benefit us all. Our values – courage, achievement, responsibility, respect, integrity, and transparency – guide us in every step we take and in every decision we make. As a company, we have a strong foundation. These fundamentals have been defined by the Merck family. We always take them into consideration when discussing and deciding on our Enterprise strategy.

- We follow a risk diversification strategy with three distinct business sectors, and we avoid overexposure to any single customer, industry, or geography. We ensure resilience against business disruption and deep crises.
- With our science and technology focus, we want to be leaders in our fields of expertise and markets, always
 pushing the boundaries to find new solutions and drive innovation. We aim to create value for our business
 and for society.
- We continue to operate under our current ownership with the Merck family as the majority owner.
- We deliver sustainable value, and we want to maintain an attractive financial profile (for example, a strong credit rating) while assessing and considering the ESG (environmental, social, governance) impact of our growth ambition.
- Mergers and acquisitions (M&A) are an important driver of our long-term value creation strategy with a focus on innovation-driven technology.

Enterprise strategy

Our ambition

Our ambition is to become the global 21st century science and technology pioneer, and we have four key priorities to deliver on this ambition.

- Mobilizing for Efficient Growth
- Leveraging Innovation in the "Big 3"1
- Driving Culture & Leadership
- Focusing on Sustainability

In all three business sectors – Life Science, Healthcare and Electronics – the course has been set for sustainable, profitable growth.

For the Life Science business sector, we expect in the medium-term growth forecast average organic sales growth of 7% to $10\%^2$ per year. The main driver will be Process Solutions, contributing around 80% to the planned growth.

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¹ As of April 1, 2022, the Big 3 include the following businesses: Process Solutions & Life Science Services in Life Science, new Healthcare products and Semiconductor Solutions in Electronics.

² Including an expected decline in pandemic-related demand

In the Healthcare business sector, we expect medium-term average annual organic sales growth in the midsingle-digit percentage range. New products should contribute around 75% to growth in the coming years up to 2025.

The Electronics business sector is now aiming to grow organically by 3% to 6% per year on average between 2021 and 2025. The Semiconductor Solutions business is to contribute around 80% to the planned growth of Electronics in the coming years.

We will continue to consistently and purposefully invest in areas that make us strong and thus aim to increase our Group sales to approximately € 25 billion by 2025. We expect Group sales to grow organically by more than 6% annually on average up to 2025. Around 80% of the planned sales growth is to come from the "Big 3" businesses – the Process Solutions business within the Life Science business sector, new products from the Healthcare business sector, as well as the Semiconductor Solutions business within the Electronics business sector.

Thanks to the rapid reduction of net financial debt, our financial flexibility is increasing significantly. For this reason, we are planning to increase total investments between 2021 and 2025 by more than 50% compared with the period from 2016 to 2020. More than 70% of this is to be invested in the "Big 3."

We will look into novel transformative technologies beyond our core products and markets while keeping in strategic proximity to our business sectors to leverage our existing assets and capabilities. Our new Group Science & Technology Office is leading the implementation of our combined strategy for innovation and "data & digital," enabling innovation across our business sectors while harnessing the power of cutting-edge data and digital capacities. It aims to identify and integrate transformative technology trends into our business sectors while maintaining a company-wide view of our tech roadmap and innovation portfolio.

We are paying particular attention to the ability of our organization to best support future growth by further developing our operating model to enable new ways of working and even quicker decision making. Moreover, our focus is on the areas of talent development and leadership culture as well as diversity and inclusion. Our voluntary aim is to achieve gender parity in leadership positions by 2030. We are also constantly working to increase efficiency regarding processes and systems as well as continuing to emphasize a culture of cost consciousness.

We have made clear progress on our sustainability strategy, incorporating sustainability even more strongly as an essential component of our corporate strategy and all company processes. For example, we have set ourselves the goal of becoming climate neutral by 2040. The Executive Board has now decided that the company will join the Science Based Targets initiative. With this step, we have committed ourselves to helping achieve the Paris Agreement goals through concrete actions.

Business strategies

Life Science

Our Life Science business sector continues to be a global leader in the $\sim \in$ 190 billion life sciences industry, consistently delivering profitable growth through a broad, differentiated portfolio, close customer relationships, solid foundational capabilities, and a well-established global footprint. These attributes, and our response to Covid-19, have strengthened our position as a trusted name and market player.

We also recognize that the life sciences are continuously evolving, with intensifying competition and key growth trends gaining momentum. To sustain our position and deliver profitable growth in the range of 7% to 10%, we have sharpened our strategic focus with a robust, multi-layered plan to achieve significant growth and profitability over the next decade.

Our plan is ambitious, with deep and far-reaching impact. Each business and function within our organization will play a critical role in executing this strategy with a rigid focus. Our newly formed Transformation Office will ensure a consistent, integrated, and milestone-driven approach. We will enhance our performance, further elevate our position as a life sciences leader and, together with our customers, impact life and health with science.

To ensure we remain differentiated as our customers' needs and expectations evolve, we will build our strong positions in consumables, capitalize on large-volume opportunities, and strengthen our go-to-market approach in academia and the Contract Research Organization area. We will augment our Lab Water business through innovation and expand our pharma QC testing offerings to biologics and novel modalities. We will continue to support products for traditional modalities, such as mAbs and high-potency-APIs as we move toward regionally-balanced manufacturing for high-growth areas like single-use and filtration.

To achieve this, we will add physical capacity and expand our manufacturing network in certain regions to grow key portfolios, leverage customer proximity and reduce business manufacturing risk. This is critical to meet the massive demand surge for our Covid-19 response while ensuring the same emphasis on the many other life-saving therapies we support. We will continue to expand in high-growth segments by building scale in attractive areas currently under-penetrated. This means investing ahead of the curve and setting the standard in new segments as they mature. For example, we will significantly scale up contract development and manufacturing organization (CDMO) activities for antibody-drug conjugates (mAbs), viral vectors, and high-potency APIs. We will also expand further into mRNA.

As we do this, we will develop new business models in areas like services and work toward creating a truly endto-end holistic offering for our customers.

We will put more emphasis on emerging regions, especially China and other Asian markets, expanding our presence to better address local market needs, establishing our company as a key partner in regional life science ecosystems.

The successful execution of our strategy will be underpinned by key enablers – innovation, digital, and resource allocation.

Accelerating innovation and focusing on science and technology leadership is essential to our future. We have embarked on a digital journey to address customer expectations and evolve our internal capabilities to drive business value, by using data science and AI tools to facilitate and automate decisions. We will continue to invest in our e-commerce platform to enable new growth models. We will target our resources toward highgrowth and high-return opportunities, including bolt-on acquisitions to augment organic efforts.

The foundation of our business is critical to all we do. Maintaining the highest quality and regulatory standards and advancing sustainability is essential to our success, and along with our people, is our greatest asset. Attracting, retaining, and developing a diverse workforce is critical to our future growth.

Healthcare

Global megatrends such as growing and aging populations as well as better access to healthcare continue to drive the need for our products. At the same time, the Covid-19 pandemic has accelerated many anticipated industry trends within the healthcare sector such as changes in market dynamics, ongoing healthcare reform, and increased digitalization. To meet these demands and respond appropriately to the dynamics of our markets, we have significantly transformed our Healthcare business sector in recent years with the objective of delivering focused leadership and sustaining above-market growth through a diversified portfolio that is resilient to long-term volatility.

Following our successes over the past years, we continue to drive pipeline projects with the aim of bringing groundbreaking medicines to patients, maximizing our existing portfolio, and continuing our expansion in growth markets. We are resolute in our ambition to become a global specialty innovator, with a high growth future in Oncology, Neurology and Immunology, and Fertility – areas where significant unmet medical needs exist and where we can bring meaningful value to patients. We build this ambition on top of a strong foundation and will continue to grow Cardiovascular, Metabolism & Endocrinology (CM&E) sustainably and profitably. We pursue this ambition with a focused leadership approach, concentrating investments on decorrelated opportunities in our pipeline and across therapeutic areas, regions, and payer types.

The first pillar of our strategy is to reinforce our global footprint, bringing the innovation of our pipeline to patients and growing our presence – in the United States and in China, for example. The emerging markets and China are expected to be the largest growth drivers for many of our established products in the future. Managing the balance between delivering innovative new medicines with first-in-class and/or best-inclass potential while leveraging our strengths in other markets and ensuring the profitable growth of the existing business will be one of the strategic imperatives. Numerous examples in our existing business offer significant opportunities to bring value to patients and considering their growth potential, maximizing their business potential will remain important.

The second pillar of our strategy is the focus on specialty medicine franchises. Here, we expect the oncology, neurology, immunology, and fertility markets to remain highly attractive in terms of size, growth prospects, and profitability. Within each specialty franchise, our approach is to develop deep internal expertise and insight, from internal research to commercialization, augmented by external talent sourcing and strategic partnering. In order to optimize the value and focus of our pipeline we continuously monitor and assess the potential of our pipeline candidates, based on clinical data, strategic fit and financial criteria, to determine the best way forward.

The third strategic pillar is innovation: We aim to develop potential first-in-class, and best-in-class therapies and to build a portfolio in each of our franchises. We have streamlined our pipeline and expanded our innovation capabilities with strong investigational drug candidates and technologies. In order to maximize the output of our R&D investments and increase our chances of success in discovering and developing new therapies, we focus our expertise on specific franchises and are exploiting synergies in disease mechanisms and biological pathways. We are investing in digital technologies and novel modalities such as antibody drug conjugates to drive pipeline growth.

Electronics

With the successful execution of the Bright Future program, our business sector has been transformed to an innovation leader within the electronics industry. In 2021, the business sector was renamed from Performance Materials to Electronics and now targets the strongly growing materials segments of the electronics industry. Our diversified portfolio delivers profitable growth and stable attractive cash flows driven by businesses like Semiconductor Solutions, Organic Light Emitting Diode (OLED) materials and future display applications. Today, our business sector is positioned as a highly appreciated innovation partner for material solutions in the semiconductor and display industries. We partner with key thought leaders around the world to enable the next generation of electronic devices.

The acceleration of digitization, and its visualization, is fueled by an exponential growth of data and a lasting need for electronics, especially semiconductor chips across all industrial sectors. Highly impactful technology trends like artificial intelligence (AI), 5G networks, big data, and Internet of Things (IoT) require more powerful chips and advanced OLED display platforms. This growth is expected to continue through the next decade, as semiconductors have become a critical component in many industries. Unprecedented investments, in the hundreds of billions of euros, are being announced for new chip manufacturing capacity across the world to overcome current chip shortages. To produce ever more powerful and energy-efficient chips, innovation in novel materials is essential.

To benefit from the strong electronics industry growth, our plan is to expand our capacities and our capabilities. We have announced investments of significantly more than \in 3 billion into innovation and capacities over the next five years aligned to the businesses and regions we serve. The investment is an essential part of our sector's new Level Up growth program to capture these opportunities.

Level Up focuses on four, mutually reinforcing key priorities: Scale, Technology, Portfolio, as well as Capabilities. The priorities Scale and Technology support the massive capacity expansion that is happening globally in our focus industries, investing in our footprint in close proximity to our customers while boosting R&D and innovation. Under the priority area Portfolio, Electronics seeks to exploit attractive, external growth opportunities via selected bolt-on acquisitions. Furthermore, Level Up will initiate or accelerate important internal initiatives under the Capabilities priority. Among other things, it will further leverage our data analytics capabilities and invest even further into the safety realm. We believe these initiatives will also strengthen our attractiveness as an employer and help further develop our talent pool.

We have a clear strategy that not only addresses semiconductor and display opportunities, but also improves resilience against market cyclicality and geopolitical impacts. Supporting this, our Surface Solutions business is again aiming for growth, after its successful restructuring. Our overall strategy for Electronics will deliver attractive financial returns, shifting towards an execution and growth phase.

Sustainability strategy

Implementing our strategy globally

Our ambition is to leverage science and technology to achieve progress for mankind. For us, sustainable entrepreneurship and profitable growth go hand in hand; we can remain competitive only by creating added value for society. Through our innovative and high-quality products, we want to help meet global challenges. At the same time, our products secure our financial performance capability.

Responsible action is an integral part of our company culture. This also includes respecting the interests of our employees, customers and investors, as well as society. For more than 350 years, our company has been shaped and guided by strong values. Our success is built on values that underpin our understanding of sustainable entrepreneurship.

The rapidly growing challenges facing society and the environment require a clear objective for the coming years. That is why we have integrated sustainability into our enterprise strategy as an essential component and have set ourselves three strategic sustainability goals: In 2030, we will achieve progress for more than one billion people through sustainable science and technology. By 2030, we will integrate sustainability into all our value chains. By 2040, we will be climate neutral and reduce our resource consumption.

In order to firmly achieve our sustainability goals, we have defined seven focus areas: sustainable innovations and technologies for our customers, impact of our technologies and products on health and well-being, sustainability culture and values, sustainability and transparency in the supply chain, securing our social license to operate in all regions, climate change and emissions, and water and resource intensity. Within these focus areas we are currently implementing numerous initiatives and projects and are measuring our progress. These efforts ensure that sustainability will become a key indicator of our success across all our business sectors. The goals we have set ourselves to 2030 and beyond will contribute to the attainment of the United Nations SDGs.

Our business activities contribute to the following five SDGs in particular: SDG 3 (Good Health and Well-Being), SDG 8 (Decent Work and Economic Growth), SDG 9 (Industry, Innovation, and Infrastructure), SDG 12 (Responsible Consumption and Production) and SDG 17 (Partnerships for the Goals).

More information on sustainability topics can be found in the non-financial statement, which for fiscal 2021 has been published in the management report for the first time.

Measuring progress made with the sustainability strategy

In 2021, we defined various key indicators in order to record and measure progress made through our three sustainability goals.

As of fiscal year 2022, we will be adding a sustainability factor to our Long-Term Incentive Plan (LTIP). The 2021 Annual General Meeting approved a revised compensation system for the members of the Executive Board. For the sustainability factor, the company uses the three key indicators marked in the table. Details on how this sustainability factor is calculated can be found in the Compensation Report.

Goal 1: In 2030, we will achieve human progress for more than one billion people through sustainable science and technology.

	ainable innovation &
tive sustainability impact tech	nologies
	be published in the SASB x as of April 12, 2022

Goal 2: By 2030, we will integrate sustainability into all our value chains.

Focus area	Sustainability key indicator	Further details
	• Percentage of women in leadership positions	Diversity & inclusion
Sustainability culture and values	 Percentage of employees trained on sustainability 	Reporting as of 2022
Sustainable and transparent supply chain	 Percentage of relevant suppliers (in terms of number and purchase volume) that are covered by a valid sustainability assessment¹ 	Responsbile supply chain
	Environment, Health and Safety (EHS) Incident Rate	Process, plant & transport safety
Securing our social license to operate in all regions	 Violations of Global Social and Labor Standards Policy 	Human rights
	Lost Time Injury Rate (LTIR)	Health & safety

¹The key indicator is used to determine the sustainability factor for the Long-Term Incentive Plan of Merck KGaA, Darmstadt, Germany (LTIP).

Goal 3: By 2040, we will achieve climate neutrality and reduce our resource consumption.

Focus area	Sustainability key indicator	Further details
	Greenhouse gas emissions (Scope 1+2) ¹	Climate action
Climate change and emissions	 Indirect greenhouse gas emissions (Scope 3) 	Climate action
	 Percentage of purchased electricity from renewable sources 	Climate action
	Waste Score	Will be published in the Sustainability Report 2021 as of April 12,2022
Water and resource intensity	Water Intensity Score	Will be published in the Sustainability Report 2021 as of April 12,2022
Water and resource intensity	Wastewater quality	Reporting as of 2022

¹The key indicator is used to determine the sustainability factor for the Long-Term Incentive Plan of Merck KGaA, Darmstadt, Germany (LTIP).

Strategic finance and dividend policy

We pursue a conservative financial policy characterized by the following:

Financial flexibility and a conservative funding strategy

We ensure that we meet our obligations at all times and adhere to a conservative and proactive funding strategy that involves the use of various financial instruments. Our diversified and profitable businesses form the basis for our strong and sustainable cash flow generation capacity. Moreover, we have several funding resources in place. A \in 2 billion syndicated loan facility is in place until 2025 to cover any unexpected cash needs.

This credit line is a backup facility that should only be used in exceptional situations. In addition, we have a commercial paper program with a volume of \notin 2 billion at our disposal. Within the scope of this program, we can issue short-term commercial paper with a maturity of up to one year.

Additionally, as a general rule, the bond market represents a key element. The most recent bond issues took place in January 2020 (\in 1.5 billion euro bonds) and September 2020 (\in 1.0 billion hybrid bond). The use of various instruments provides a broad financing basis and addresses different investor groups.

Maintaining long-term and reliable business relations with a core group of banks

We mainly work with a well-diversified, financially stable and reliable group of banks. Due to our long-term business approach, bank relationships typically last for many years and are characterized by professionalism and trust. The banking group consists of banks with strong capabilities and expertise in various products and geographical regions. We regard these banks as strategic partners and involve them in important financing transactions accordingly.

Strong investment-grade rating

The rating of our creditworthiness by external rating agencies is an important indicator of financial stability. A strong investment-grade rating is an important cornerstone of our financial policy, as it safeguards access to capital markets at attractive financial conditions. On October 21, 2021, we received a rating upgrade by Moody's from Baa1 to A3 (stable outlook). In October 2021, Scope Ratings also changed the outlook of our A-rating from stable to positive. The Standard & Poor's (S&P) rating is A with a stable outlook.

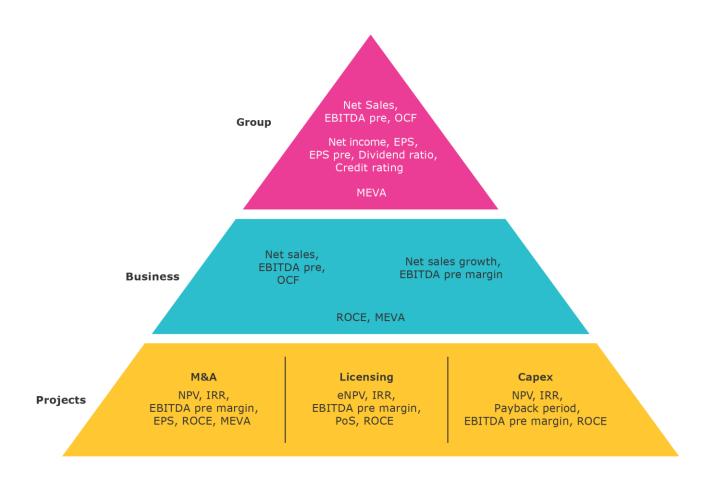
Sustainable dividend policy

We are pursuing a sustainable dividend policy. Provided the economic environment develops in a stable manner, the current dividend represents the minimum level for future dividend proposals. Our dividend policy will follow business development and earnings increases over the coming years. However, dividend growth could deviate, for example, within the scope of restructuring or in the event of significant global economic developments. We aim for a target corridor of 20% to 25% of earnings per share pre.

Internal Management System

As a global company with a diverse portfolio of products and services, we use a comprehensive framework of indicators to manage performance. The most important key performance indicator (KPI) for measuring performance is EBITDA pre¹.

The Value Creation and Financial KPI Pyramid, which summarizes our important financial performance measures, reflects the comprehensive framework of financial KPIs to steer the businesses and prioritize the allocation of cash resources. It consists of three managerial dimensions: Group, Business, and Projects, each of which requires the use of different indicators.



Abbreviations

EBITDA pre = Earnings before interest, income tax, depreciation and amortization as well as adjustments. EPS = Earnings per share. MEVA¹ = Value added of Group. OCF^1 = Operating Cash Flow. $ROCE^1$ = Return on capital employed. NPV^1 = Net present value. IRR^1 = Internal rate of return. $eNPV^1$ = Expected Net present value. POS^1 = Probability of success. $M&A^1$ = Mergers & Acquisitions.

 $^{\rm 1}$ Not defined by International Financial Reporting Standards (IFRS).

Key performance indicators of the Group and its businesses

The three key performance indicators of net sales, EBITDA pre, and operating cash flow (OCF) are the most important factors for assessing operational performance. Therefore, we refer to these KPIs in the Report on Economic Position, the Report on Risks and Opportunities, and the Report on Expected Developments. As the most important indicators of financial business performance, the KPIs are key elements of our performance management system.

Net sales

Net sales are defined as the revenues from the sale of goods, services rendered to external customers, and commission income and profit sharing from collaborations, net of value-added-tax, and after sales deductions such as rebates or discounts. Net sales are the main indicator of our business growth and therefore an important parameter of external as well as internal performance measurement. In addition, organic sales growth compared with the operating plan is used for internal performance management. Organic sales growth shows the percentage change in net sales versus a comparative period, adjusted for exchange rate and portfolio effects. Exchange rate effects may arise as a result of foreign exchange fluctuation between the functional non-euro currency of a consolidated company and the reporting currency (euro). By contrast, portfolio effects reflect sales changes due to acquisitions and divestments of consolidated companies or businesses.

€ million	2021	2020	Change € million	%
€ million	19,687	2020 17,534	€ million 2,152	<u>%</u> 12.3%

EBITDA pre

EBITDA pre is the main performance indicator measuring ongoing operational profitability and is used internally and externally. To provide an alternative understanding of the underlying operational performance, it excludes from the operating result depreciation and amortization, impairment losses and reversals of impairment losses, as well as adjustments. These adjustments are restricted to the following categories: integration expenses, IT expenses for selected projects, restructuring expenses, gains/losses on the divestment of businesses, acquisition expenses, and other adjustments. The classification of specific income and expenses as adjustments follows clear rules and underlies strict governance at the Group level. Within the scope of internal performance management, EBITDA pre allows for necessary changes or restructuring without penalizing the performance of the operating business. The following table shows the composition of EBITDA pre in the 2021 fiscal year compared to the previous year. The IFRS figures have been modified to reflect the elimination of adjustments included in the respective functional costs.

Group

Reconciliation EBITDA pre¹

Reconciliation EDITIDA pre		2021			2020²		Change
		Elimination of			Elimination of		
€ million	IFRS	adjustments	pre ¹	IFRS	adjustments	pre ¹	pre ¹
Net sales	19,687	-	19,687	17,534	-	17,534	12.3%
Cost of sales	-7,351	25	-7,326	-6,835	53	-6,782	8.0%
Gross profit	12,335	25	12,361	10,699	53	10,752	15.0%
Marketing and selling expenses	-4,304	17	-4,287	-4,207	60	-4,147	3.4%
Administration expenses	-1,241	83	-1,158	-1,188	98	-1,090	6.3%
Research and development costs	-2,408	8	-2,400	-2,288	27	-2,262	6.1%
Impairment losses and reversal of impairment losses on financial assets (net)	1		1	-6	-0	-6	>100.0%
Other operating income and expenses	-206	76	-129	-25	169	144	>100.0%
Operating result (EBIT) ¹	4,179			2,985			
Depreciation/amortization/ impairment losses/reversals of impairment losses	1,767	-53	1,715	1,938	-128	1,810	-5.3%
EBITDA ²	5,946			4,923	·		
Restructuring expenses	79	-79		162	-162	_	
Integration expenses/IT expenses	81	-81		108	-108	-	
Gains (-)/losses (+) on the divestment of businesses	-3	3		10	-10	-	
Acquisition-related adjustments	-18	18		-10	10	_	
Other adjustments	19	-19		9	-9	_	
EBITDA pre ¹	6,103		6,103	5,201		5,201	17.3%
thereof: organic growth ¹							18.1%
thereof: exchange rate effects						-	-0.6%
thereof: acquisitions/divestments						-	-0.1%

¹ Not defined by International Financial Reporting Standard (IFRS).

² Not defined by International Financial Reporting Standards (IFRS); EBITDA corresponds to operating result (EBIT) adjusted by depreciation, amortization, impairment losses, and reversals of impairment losses.

Operating cash flow (OCF)

As announced in the annual report 2020, the Operating Cash Flow has been introduced as leading steering KPI for us since the beginning of 2021. The Operating Cash Flow results from our running business and describes the cash generated by operations. It is mainly influenced by the EBITDA pre, income tax, financial result and changes in net working capital.

Group

			Change	2
€ million	2021	2020	€ million	%
EBITDA pre ¹	6,103	5,201	901	17.3%
Adjustments ¹	-157	-279	122	-43.7%
Finance result ²	-255	-354	100	-28.1%
Income tax ²	-859	-637	-222	34.9%
Changes in other financial assets recognized in profit or loss	-6	0	-6	>100.0%
Changes in working capital ¹	-349	-162	-186	>100.0%
thereof: Changes in inventories ³	-472	-85	-387	>100.0%
thereof: Changes in trade accounts receivable ³	-310	-84	-226	>100.0%
thereof: Changes in trade accounts payable/refund liabilities ³	433	7	426	>100.0%
Changes in provisions ³	196	-110	305	>100.0%
Changes in other assets and liabilities ³	-121	-123	2	-2.0%
Meutralization of gains/losses on disposal of fixed assets and other disposals ³	-24	-98	74	-75.7%
Other non-cash income and expenses ³	86	39	48	>100.0%
Operating cash flow	4,616	3,477	1,138	32.7%

 $^{\rm 1}$ Not defined by International Financial Reporting Standard (IFRS).

 $^{\rm 2}$ According to Consolidated Income Statement.

³ According to the Consolidated Cash Flow Statement.

Sustainable value creation is essential to secure the long-term success of the company. To optimize the allocation of financial resources, we use a defined set of parameters as criteria for the prioritization of investment opportunities and portfolio decisions.

Net present value (NPV)

The main criterion for the prioritization of investment opportunities is the net present value. It is based on the discounted cash flow method and is calculated as the sum of the discounted free cash flows over the projection period of a project. The weighted average cost of capital (WACC), representing the weighted average of the cost of equity and cost of debt, is used as the discount rate. Depending on the type and location of a project, different markups are applied to the WACC.

Internal rate of return (IRR)

The internal rate of return is a further important criterion for the assessment of acquisition projects and investments in property, plant and equipment, as well as intangible assets. It is the discount rate that makes the present value of all future free cash flows equal to the initial investment or the purchase price of an acquisition. A project adds value if the internal rate of return is higher than the weighted cost of capital including markups.

Return on capital employed (ROCE)

In addition to NPV and IRR, when looking at individual accounting periods, return on capital employed is an important metric for the assessment of investment projects. It is calculated as the adjusted operating result (EBIT) pre divided by the sum of property, plant and equipment, intangible assets, trade accounts receivable, trade accounts payable, and inventories.

Payback period

An additional parameter to prioritize investments in property, plant & equipment, and intangible assets is the payback period, which indicates the time in years after which an investment will generate positive net cash flow.

Value added of Group (MEVA)

Value added of Group gives information about the financial value created in a period. Value is created when the return on capital employed (ROCE) of the company or the business is higher than the weighted average cost of capital (WACC). MEVA metrics provide us with a powerful tool to weigh investment and spending decisions against capital requirements and investors' expectations.

Capital market-related parameters

Net income, earnings per share (EPS), and earnings per share pre (EPS pre)

Earnings per share are calculated by dividing profit after tax attributable to the shareholders of Merck KGaA, Darmstadt, Germany (net income) by the weighted average number of theoretical shares outstanding. The use of a theoretical number of shares takes into account the fact that the general partner's capital is not represented by shares. To provide an alternative view, we also report earnings per share pre, in which the effects of integration expenses, IT expenses for selected projects, restructuring expenses, gains/losses on the divestment of businesses, acquisition expenses, and other adjustments are eliminated. Moreover, amortization of acquired intangible assets as well as impairment losses on property, plant & equipment, and intangible assets are eliminated. The adjustment excludes impairment losses on intangible assets for acquired research and development (R&D) projects below a threshold value of \in 50 million. Income tax is calculated on the basis of the company's underlying tax rate. The following table presents the reconciliation of net income to net income pre for the calculation of EPS pre.

Reconciliation net income to net income pre¹

			Change	
€ million	2021	2020	€ million	in %
Net income	3,055	1,987	1,067	53.7%
Non-controlling interest	10	7	4	58.5%
Income tax	859	637	222	34.9%
Amortization of acquired intangible assets	803	857	-54	-6.3%
Adjustments ¹	210	407	-197	-48.5%
Income tax on the basis of the underlying tax rate ¹	-1,135	-974	-162	16.6%
Non-controlling interests to be adjusted	-10	-7	-4	58.5%
Net income pre ¹	3,791	2,914	876	30.1%
Earnings per share pre ¹ in €	8.72	6.70	2.02	30.1%

¹ Not defined by International Financial Reporting Standards (IFRS).

Credit rating

The rating of our creditworthiness by external agencies is an important indicator of our ability to raise debt capital at attractive market conditions. The capital market makes use of the assessments published by independent rating agencies in order to assist debt providers in estimating the risks associated with a financial instrument. We are currently assessed by Moody's, Standard & Poor's, and Scope. The most important factor for the credit rating is the ability to repay debt, which is determined in particular by the ratio of operating cash flow to net- or gross financial debt.

Dividend ratio

We pursue a reliable dividend policy with a target payout ratio based on EPS pre (see definition above) with the aim of ensuring an attractive return for our shareholders.

Other relevant/non-financial performance measures

Along with the indicators of the financial performance of the businesses, non-financial measures also play an important role in furthering the success of the company. From a Group perspective, innovations in the businesses as well as the promotion of a diverse workforce, especially at the leadership level, and sustained planning for the filling of company-critical positions, are of particular importance.

Innovation

Innovations are the foundation of our business and will also be prerequisites for future success in changing markets. We are continuously working to develop new products and service innovations for patients and customers. Indicators for the degree of innovation are defined based on the specifics of the respective businesses.

Sustained employee development

We believe that a diverse workforce strengthens our ability to innovate. We actively promote diversity among our leaders in order to create an integrative culture that reflects our values and enables every employee to fulfill their potential. We ensure that our ambitious corporate goals can be realized through strategic succession planning for company-critical positions. To gauge the success of the related measures, we have introduced diversity and succession planning as focus issues and non-financial indicators.

Research and Development

Science is at the heart of everything we do. We conduct research and development (R&D) worldwide in order to develop new products and services to improve the quality of life of patients and satisfy the needs of our customers. Further optimizing the relevance and efficiency of our research and development activities – either on our own or in cooperation with third parties – is one of our top priorities.

Around 8,300 employees worked in research and development and corresponding support functions in 2021. They dealt with innovations to address long-term health and technology trends in both established and growth markets (2020: approximately 7,900).

Expenditures for R&D amounted to € 2.4 billion in 2021 (2020: € 2.3 billion). The organizational setup of our R&D activities reflects our structure with three business sectors. In the Life Science business sector, our research activities focus on developing innovative technologies for laboratory and life science applications in government and academic labs, the biopharmaceutical industry and the industrial sector. We continue to focus on digitized and automated labware, DNA purification for downstream applications, and emerging chemical synthesis, as well as software for our BioContinuum[™] Platform to accelerate Biopharma 4.0. In addition, our teams remain dedicated to delivering advancements in our core portfolios, such as filtration, pure lab water, and diagnostic solutions. With our Healthcare business sector's R&D pipeline, we aspire to make a positive difference for patients – always with the goal to help create, improve, and prolong lives. Our main research areas include oncology, immuno-oncology, and immunology including multiple sclerosis. The main focus of our Electronics business sector's research is on the development of innovative materials and technologies required for the manufacturing of ever smaller, faster and more powerful processors and memory chips. In addition, Electronics develops novel materials for next-generation displays and functional and decorative effect pigments for use in the automotive and cosmetics industries and other industrial applications.

			Change	
€ million	2021	2020	€ million	%
Life Science	351	313	38	12.1%
Healthcare	1,712	1,640	72	4.4%
Electronics	278	274	4	1.6%
Corporate and Other	67	62	5	8.4%
Total	2,408	2,288	119	5.2%

Research and Development Costs

The ratio of research expenditure to Group sales was 12.2% (2020: 13.0%). The decline is due to the positive sales development.

Life Science*

Across our three business units of Research Solutions, Process Solutions and Applied Solutions, our R&D teams, composed of approximately 2,000 employees, continue to bring expertise and a diversified and relevant portfolio of products and services to our customers around the world. In 2021, our Life Science business sector focused on delivering breakthrough innovations for our academic, biopharmaceutical and industrial customers.

As such, we launched more than 15,000 products in 2021, including those launched through our "faucet program" for antibodies, reference materials, chemicals and nanomaterials. These included key innovations from all our business units, such as our GenElute[™]-E Single Spin purification kits; ProCellics[™] Raman Analyzer with Bio4C[™] PAT Raman Software, and a new Milli-Q[®] EQ 7000 Type 1 water purification system.

Research Solutions

In May, we introduced a new solution improving productivity in the lab through a more flexible and streamlined nucleic acid purification process. GenElute[™]-E kits reduce traditional silica-based workflow hands-on time from about 45 minutes to only three minutes. The technology workflow also reduces plastic waste on average by 55%, compared with traditional methods, and eliminates overnight processing requirements.

In September, the Millicell[®] DCI Digital Cell Imager was introduced for fast, accurate, and objective cell monitoring. Besides assessing common cell culture parameters and growth trends for more consistent cell cultures, it expands capabilities with off-device cloud storage and a web-based app for data analysis, sorting, and archiving. With the instrument, it's possible to collect critical insights without risking sample contamination from manual cell culture handling.

Also in September, we introduced the ColorWheel[®] flow cytometry antibodies and dyes, a lyophilized product for enhanced stability and ambient shipping that allows for more flexibility for scientists to pair any antibody with any dye in their flow cytometry workflows.

Process Solutions

In March, we received a patent for an improved CRISPR genome-editing method in Japan. Our proxy-CRISPR technology provides a solution to improve genome editing and advance new possibilities for research. This marks our second CRISPR patent in Japan and our 38th CRISPR patent. Our 39th and 40th CRISPR patents were also allowed in May by the European Patent Office and the Intellectual Property Office of Singapore, respectively, which are directed to our CRISPR-chrom and CRISPR vector technologies.

In September, we launched the ProCellics[™] Raman Analyzer with Bio4C[™] PAT Raman Software, continuing to pave the way to Bioprocessing 4.0. This new time-saving product, which won the "Best New Product/Service" award at Interphex 2021, enables greater upstream process optimization, helps reduce the risk of contamination and batch failures and provides added flexibility to operators.

In October, we launched the new technology Chetosensar[™], giving new promise to antibody-drug conjugates (ADC) that were previously terminated by alleviating the solubility challenges and expanded capacity to advance ADC therapies. These initiatives underscore our continued investment in novel modalities and support our efforts to double our ADC and High-Potent Active Pharmaceutical Ingredient (HPAPI) capacity in the near future.

In October, we also signed an agreement licensing our patented CRISPR-Cas9 technology to Cellecta, Inc., a functional genomics products and services provider based in Mountain View, California, United States. Through the licensing of its innovative technology, we are paving the path for researchers and scientists to identify and accelerate next generation treatments. Cellecta provides RNAi and CRISPR technologies for the discovery and characterization of novel therapeutic targets and genetic profiling for drug and biomarker discovery and

validation, leading the way for developing highly effective next-generational treatments. Cellecta plans to use the foundational CRISPR patent estate for CRISPR-mediated targeted "knock-in", a critical method that gives scientists more efficient options for complex projects in therapeutic and disease research.

In November, we signed a Memorandum of Understanding (MoU) with the Korea-based bio-venture company, GI Innovation, to further research and development of critical life-saving cancer treatments, as well as drugs for allergy-related conditions. Through the mutual agreement, we will support GI Innovation with technologies and services including CHOZN[®] platform, cell culture media, and overall process consulting and technical support.

In December, we announced a strategic collaboration with biotechnology companies Innovative Biotech to design the manufacturing process for the first vaccine production facility in Nigeria.

Applied Solutions

In January, we launched the new Milli-Q[®] EQ 7000 Type 1 water purification system to expand our benchtop ultrapure water system portfolio. The new Milli-Q[®] EQ 7000 system produces consistent ultrapure water quality that is easily customized to experimental requirements, strengthening our Milli-Q[®] ultrapure water offering.

The \in 35 million expansion project to build a second lateral flow membrane manufacturing product line in Cork, Ireland, was completed this year, and commercial manufacturing commenced over the summer. The new casting line more than doubles our lateral flow membrane capacity.

Additionally, earlier this year, three of our Milli-Q[®] water purification systems were designated Greener Alternative Products. The Milli-Q[®] IQ 7000, IQ 7003, and IQ 7010 water purification systems were innovated not only to be more compact but also to use less water, plastic, and electricity.

In December, the U.S. government awarded a \in 121 million contract (\$136.7 USD) for the construction of a lateral flow membrane production facility, over a three-year period, at the company's United States site in Sheboygan, Wisconsin. The contract, received 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.

Recognized for Award-Winning Innovation

In April, we were named 2021 Charitable Supplier of the Year and 2021 Protein Supplier of the Year by the CiteAb Awards. These awards, from a leading life science data provider, celebrate the top suppliers and individuals in the research reagent sector worldwide, helping researchers and their suppliers make more informed decisions.

In June, our Madison, Wisconsin, United States, site was awarded "Best New HPAPI Facility" at the 2021 HPAPI Summit. This new 70,000-square-foot facility doubles our HPAPI kilo lab capacity and enables us to expedite the manufacture of HPAPIs, ADC linker/payloads, and complex APIs. With our new expanded facility, we will be the largest single-digit occupational exposure limit CDMO provider in the world.

In September, we signed a partnership with the Federal University of Goiás State, Brazil to create an Innovation and Technology Hub. The partnership will enable the implementation of a prototyping and a training center for rapid diagnostic tests. The new space is the first in Brazil to concentrate molecular biology techniques, electrochemical biosensors and rapid tests by lateral flow immunochromatography in one laboratory.

In November, we announced that we will support SaudiVax Ltd., based in the Kingdom of Saudi Arabia, to design a best-in-class, multi-modality manufacturing facility to localize manufacturing of biologics and vaccines for the MENA region. SaudiVax is positioned to become the first developer and manufacturer of Halal vaccines and biotherapeutics in Saudi Arabia, leveraging our integrated Contract Development Manufacturing Services (CDMO), innovative product offerings and single-use technologies.

Healthcare*

With our Healthcare research pipeline, we aspire to make a positive difference for patients – always with the purpose to help create, improve, and prolong lives. Our main research focus areas include oncology, neurology, and immunology.

Neurology & Immunology

Multiple sclerosis (MS) is one of the world's most common neurological disorders. Despite the emergence of a number of therapies in the last two decades, there are still significant unmet needs for MS patients. As a company we have more than 20 years of experience in MS research, and we remain committed to finding solutions for patients' significant unmet medical needs in this area.

New data for both our marketed MS treatments Mavenclad[®] (cladribine tablets) and Rebif[®] (interferon beta-1a), and our investigational treatments evobrutinib and enpatoran, have been presented across key congresses in 2021, including the Americas Committee for Treatment and Research in Multiple Sclerosis (ACTRIMS) Forum 2021 in February and the 2021 American Academy of Neurology (AAN) Annual Meeting in April. Generating data around our MS treatments and the risk of respiratory viral infections has remained important in 2021, helping to support clinicians as they make treatment decisions for their patients living with MS during the Covid-19 pandemic. At ACTRIMS, we presented new data from the MAGNIFY-MS study, indicating that Mavenclad-treated relapsing multiple sclerosis (RMS) patients mount a protective antibody response to common vaccines. The MAGNIFY-MS retrospective analysis demonstrated that patients develop protective antibody levels for at least six months following seasonal influenza and varicella zoster vaccines, irrespective of vaccine timing relative to Mavenclad-dosing.

At AAN, we announced a new analysis from the MAGNIFY-MS sub-study showing a specific immune repopulation pattern in patients with RMS treated with Mavenclad[®], which may contribute to their ability to fight infections and develop protective antibodies from vaccines. In addition, an independent study conducted by Anat Achiron, MD, PhD, FAAN, and colleagues, The Multiple Sclerosis Center at Sheba Medical Centre and Sackler School of Medicine Tel Aviv University, Israel, was published in the "Therapeutic Advances in Neurological Disorders" journal in April and also presented at the AAN congress, showing that patients on Mavenclad-treatment were able to generate Covid-19 antibodies following the mRNA vaccine from Pfizer/BioNTech. Humoral response to the Covid-19 vaccine was independent of lymphocyte count.

Also presented at AAN were data from a Phase II placebo-controlled randomized trial showing that evobrutinib significantly reduced blood neurofilament light chain (NfL) levels, a key biomarker of neuronal damage and inflammation, in patients with MS. Elevated blood NfL levels have been shown to be associated with damage to neurons and may predict future brain atrophy and disease progression.

Enpatoran, a highly specific potential first-in-class immune modulator blocking the activation of Toll-like receptor (TLR)7 and TLR8, was the focus of two presentations at major lupus and infectious disease congresses, including ID WEEK 2021 in September and LUPUS & CORA 2021 in October. Enpatoran is being developed as a potential new oral therapy for systemic lupus erythematosus (SLE) and cutaneous lupus erythematosus (CLE), and aims to overcome limitations of available lupus therapies by providing selective inhibition of lupus-relevant disease drivers, which may increase efficacy while preserving immunity against infections. Initiation of Phase II studies in SLE and CLE is expected in the first half of 2022.

We presented a total of 39 abstracts at the 37th Congress of the European Committee for Treatment and Research in Multiple Sclerosis (ECTRIMS) in October. Among the presentations were late-breaking real-world data on Mavenclad[®], showing a sustained benefit on long-term mobility and disability status. New data also highlighted improvement in measures of physical and mental health after one year of Mavenclad[®]-treatment,

plus new independent data that continued to show Mavenclad[®]-treated patients receiving an mRNA Covid-19 vaccine mount a similar antibody response similar to that of the general population.

New evobrutinib data were also presented at ECTRIMS, showing that evobrutinib was effective at reducing the volume of slowly expanding lesions (SEL), an imaging biomarker of chronic active inflammation and axonal loss within the central nervous system (CNS), making it the first Bruton's tyrosine kinase (BTK) inhibitor to show a significant effect on this biomarker. Additionally, new safety data from the first and only integrated safety analysis of a BTK inhibitor that included MS patients were also presented, showing that evobrutinib was generally well tolerated. This came shortly after the announcement of evobrutinib being the first BTK inhibitor to complete Phase III trial enrollment.

We have continued to deliver on the strategic evolution of our immunology pipeline this year, allowing us to focus our efforts on priority assets and areas of expertise to deliver the greatest impact for patients. In May, we announced the completion of an out-licensing agreement with MoonLake Immunotherapeutics AG, Switzerland, for sonelokimab (M1095). Sonelokimab is an investigational anti-IL-17 A/F Nanobody[®], which neutralizes both IL-17A and IL-17F, in patients with moderate to severe chronic plaque-type psoriasis. In January 2022 we out-licensed sprifermin, a recombinant form of human fibroblast growth factor 18, to HighLine Bio Inc, a company newly established by TrialSprak. Sprifermin is being investigated in osteoarthritis, and TrialSpark/HighLine Bio will assume full responsibility for the research, development and commercialization of the asset.

In December we announced a strategically focused expansion of our neuroinflammatory pipeline with the acquisition of the rights to develop cladribine for the treatment of generalized myasthenia gravis (gMG) and neuromyelitis optica spectrum disorder (NMOSD).

Oncology

Oncology is a core focus area in our R&D portfolio. With an emphasis on biology-driven research, we aim to deliver transformative treatments. Translational research is embedded into the whole R&D process, with several projects addressing unmet needs in hard-to-treat cancers through innovative treatment approaches and novel combinations. In 2021, we achieved several milestones across our oncology pipeline.

We continue to develop much-needed new treatment options for patients with hard-to-treat cancers and have made key progress in this area with Bavencio[®] (avelumab), an anti-PD-L1 antibody we are co-developing and co-commercializing with Pfizer Inc., United States. On January 25, the European Commission approved Bavencio[®] as monotherapy for the first-line maintenance treatment of adult patients with locally advanced or metastatic urothelial carcinoma (UC) who are progression-free following platinum-based chemotherapy. Bavencio[®] was first approved in the United States as a first-line maintenance treatment for advanced UC by the U.S. Food and Drug Administration (FDA) in June 2020 and is now approved for this indication in 50 countries. It is also approved as a monotherapy for the treatment of metastatic Merkel cell carcinoma in 55 countries and for the treatment of advanced renal cell carcinoma in combination with axitinib in 50 countries.

Other highlights from our development pipeline included the advancement of several potential first-inclass/best-in-class compounds. The development program for tepotinib, our oral MET inhibitor designed to inhibit the oncogenic MET receptor signaling caused by *MET* (gene) alterations, has continued to achieve multiple milestones in 2021. Discovered in-house at our company, tepotinib underscores our strategic focus on delivering innovative precision medicines to patients with cancer. In February 2021, the FDA granted accelerated approval to tepotinib under the brand name Tepmetko[®], making it the first and only once-daily oral MET inhibitor approved for patients with metastatic non-small cell lung cancer (NSCLC) with *MET*ex14 skipping alterations. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials. In December 2021, Tepmetko became the first and only oral MET inhibitor to receive the Committee for Medicinal Products for Human Use (CHMP) positive opinion in Europe for adult patients with advanced NSCLC harboring alterations leading to *MET*ex14 skipping. Tepotinib is now available in a number of countries, and under review by other regulatory authorities globally. On April 12, we announced initiation of a Phase II trial with registrational intent for berzosertib, the leading asset in the Company's DNA damage response (DDR) inhibitor development program. The berzosertib clinical development program is one of the most advanced Ataxia telangiectasia and rad3-related (ATR) inhibitor development programs industry-wide. The global study will further assess berzosertib in combination with topotecan for the treatment of relapsed, platinum-resistant SCLC (DDRiver SCLC 250) and plans to include approximately 80 participants at about 41 study sites across Asia, Europe, and North America. As part of its new DDRiver[™] Clinical Trials program, the Company is investigating DDR inhibitor targeting pathways across more than ten trials in various tumor types. Results from a Phase II proof-of-concept study conducted by the US National Cancer Institute (NCI) (NCT02487095) were also published in the April 12, 2021 edition of Cancer Cell showing that berzosertib in combination with the chemotherapy topotecan resulted in an objective response rate (ORR) of 36% among patients with relapsed small cell lung cancer (SCLC), including durable responses among a majority of responding patients with platinum-resistant disease. Berzosertib, formerly known as VX-970, was licensed from Vertex Pharmaceuticals in 2017.

At the 2021 American Society of Clinical Oncology (ASCO) Annual Virtual Meeting held June 4-8, we had a significant presence with 40 abstracts including seven oral presentations and seven poster discussions at the Virtual Scientific Program. Potential first-in-class/best-in-class early- and late-stage pipeline compounds, and investigational uses of our approved medicines were featured at the meeting.

For Bavencio[®], data provided further evidence of continued patient benefit across three approved indications and included:

- New analyses from the Phase III JAVELIN Bladder 100 study demonstrating consistent survival benefit of Bavencio[®] as first-line maintenance treatment across key subgroups further reinforcing the role of Bavencio[®] for patients with advanced UC that have not progressed on 1L platinum-containing chemotherapy (abstracts: #4520; #4525; #4527).
- In advanced renal cell carcinoma (aRCC), data confirmed the efficacy benefits of the combination of Bavencio[®] plux axitinib across International Metastatic RCC Data Consortium (IMDC) risk groups including in the favorable risk group from the extended follow-up of the Phase III JAVELIN Renal 101 study (abstracts: #4514; #4574)
- More than five years of follow-up in Part A of the Phase II JAVELIN Merkel 200 study in metastatic Merkel cell carcinoma (mMCC) (#9517) showed meaningful long-term overall survival in previously treated patients with metastatic MCC (mMCC) who were treated with Bavencio[®], supporting its role as a standard of care for these patients.

For tepotinib, new data from the Phase II VISION study was presented including:

- An oral presentation on *MET*ex14 NSCLC biomarker response detected in liquid biopsy (#9012); this investigation provides evidence that liquid biopsy may provide a reliable means for monitoring.
- *MET*ex14 skipping NSCLC with brain metastases (abstract #9084) where data demonstrated efficacy in patients with *MET*ex14 skipping NSCLC with brain metastases consistent with the overall treatment population, brain metastases are reported in 20% to 40% of patients with *MET*ex14 skipping NSCLC and are associated with poor prognosis.
- NSCLC with *MET* amplification (*MET*amp) (abstract #9021) in VISION Cohort B, the first study of a MET inhibitor in people with NSCLC with *MET*amp prospectively detected by liquid biopsy, showed the potential of tepotinib to target *MET*amp-driven disease. *MET* amplification is a genetic alteration occurring in approximately 1% to 5% of patients with NSCLC and has no approved targeted therapies.

For our first biology-driven leader, Erbitux[®] (cetuximab), a number of Investigator Sponsored Studies (ISS) continue to demonstrate its steady role across the continuum of care in mCRC, and as a backbone of treatment in squamous cell carcinoma of the head and neck. We licensed the right to market Erbitux[®], a registered trademark of ImClone LLC, outside the United States and Canada from ImClone LLC, a wholly owned subsidiary of Eli Lilly and Company, in 1998.

At the IASLC 2021 World Conference on Lung Cancer (WCLC) and the European Society of Medical Oncology (ESMO) Annual Virtual Meetings in September 2021, we presented 27 abstracts on research from Companysponsored, investigator-sponsored, and collaborative studies — including two oral and two mini-oral presentations.

For Bavencio[®], real-world evidence was presented supporting the continued need for first-line treatments for advanced urothelial carcinoma (abstracts: #701P; #706P; #707P). Data from an investigator-sponsored study of avelumab in combination with neoadjuvant chemotherapy to treat muscle-invasive bladder cancer was also presented for the first time (presentation #659MO).

Data for tepotinib at the WCLC (abstracts: #P45.03; #P51.01) and ESMO (abstracts: #1254P; #1255P; #1366TIP) included the VISION trial — the largest study of patients with *MET*ex14 skipping NSCLC prospectively enrolled based on liquid and/or tissue biopsy (n=275) and, a trial-in-progress update from the ongoing INSIGHT 2 study in EGFR-mutant NSCLC with *MET* amplification.

Erbitux[®] (cetuximab) data at ESMO continue to demonstrate, in a number of studies, its significant role as the backbone of treatment in mCRC (abstract #415P; presentation #387MO).

For our investigational ATR inhibitor berzosertib (M6620), a first-time look at the ongoing Phase II study of berzosertib in patients with relapsed platinum-resistant small cell lung cancer (SCLC) was presented (abstract #1666TIP).

On September 30, we announced a mutual decision to end the global strategic alliance with GlaxoSmithKline plc, United Kingdom, (GSK) to develop bintrafusp alfa, the investigational bifunctional fusion protein designed to simultaneously block TGF- β and PD-L1. This decision was based on the clinical trial data generated to date, including three randomized clinical trials that did not demonstrate a benefit to patients.

In January, we made the decision to discontinue the INTR@PID Lung 037 clinical trial in the first-line treatment of patients with stage IV NSCLC that have high expression of PD-L1, based on the recommendation of the Independent Data Monitoring Committee, as the study was unlikely to meet the co-primary endpoint, specifically progression-free survival.

Top-line data announced in March from the Phase II INTR@PID BTC 047 study evaluating bintrafusp alfa as a monotherapy in the second-line treatment of patients with locally advanced or metastatic biliary tract cancer (BTC) who have failed or are intolerant of first-line platinum-based chemotherapy showed single-agent activity, though the study did not meet the predefined threshold that would have enabled regulatory filing for BTC in the second-line setting.

In August, based on a review of data conducted by the Independent Data Monitoring Committee, we decided to discontinue the Phase II INTR@PID BTC 055 study evaluating bintrafusp alfa with gemcitabine plus cisplatin in the first-line treatment of patients with locally advanced or metastatic biliary tract cancer (BTC), as the study was unlikely to achieve the primary objective of overall survival.

Based on these findings, several remaining studies in the program were discontinued, including those in nonsmall cell lung cancer, triple negative breast cancer, biliary tract cancer, and bladder cancer. To augment the in-house innovations in our oncology portfolio with potential new solutions for patients with cancer, we announced in March 2021 that we entered into a worldwide in-licensing agreement with Debiopharm, Switzerland, for the worldwide development and commercialization of xevinapant (Debio 1143). Xevinapant, a potent oral antagonist of Inhibitor of Apoptosis Proteins (IAP), 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.

Fertility

In a step forward for women with severe follicle-stimulating hormone (FSH) and luteinizing hormone (LH) deficiency and their treating physicians, in October 2021 the Committee for Medicinal Products for Human Use (CHMP) recommended an update to the Summary of Product Characteristics (SmPC) for Pergoveris[®]. Current scientific and clinical knowledge regarding the nature and attributes of FSH LH and LH deficiency show that severe FSH and LH deficiency cannot be defined using specific cut-off levels of FSH and LH clinical indicators. The SmPC update ensures better clarity for healthcare professionals (HCPs) on when to dispense Pergoveris[®].

The 2021 meeting of the European Society of Human Reproduction and Embryology (ESHRE) that was taking place in June, saw three abstracts presented, including one oral presentation that highlighted comparative real-world effectiveness data of assisted reproduction technology collected in the National Health database in France, for women stimulated by different gonadotropins, including Gonal-f[®], which showed positive clinical outcomes like cumulative live birth rate. Additionally, seven high-priority fertility manuscripts have been published in top-quartile journals so far.

A meta-analysis published in April 2021¹ suggested positive outcomes for the reference product Gonal-f[®] compared to treatment with biosimilar preparations of follitropin alfa regarding probability of live birth, as well as clinical and ongoing pregnancy. In addition, safety data showed for biosimilars and reference product a similar risk of ovarian hyperstimulation syndrome (OHSS), ectopic pregnancy, and multiple pregnancy¹. The evidence base for Gonal-f[®] was further strengthened by a real-world study published in June 2021², which showed that treatment with Gonal-f[®] resulted in higher rates of cumulative live birth, cumulative ongoing, and cumulative clinical pregnancy versus highly purified human menotropin (HP-hMG).

We continue to support efforts to save the northern white rhinoceros from extinction. We are a partner of the BioRescue Project of the Leibniz Institute for Zoo and Wildlife Research (Leibniz-IZW) in the Forschungsverbund Berlin e.V., donating technology and financial support, as well as sharing expertise and experience in fertility to their work.

Cardiovascular Metabolism & Endocrinology (CM&E)

The new formulation of Euthyrox[®] (levothyroxine) for the treatment of hypothyroidism obtained further regulatory approvals in 2021, resulting in a total of 80 countries where this incremental innovation is registered, allowing for more precise dosing.

Glucophage[®], containing the active ingredient metformin, is the drug of choice for first-line treatment of type 2 diabetes available in more than 100 countries. It is also approved in 89 countries for prediabetes when lifestyle intervention is not enough to control the condition. With the successful submission and launch of Glucophage[®] XR 850, a new dose strength has been developed for the Glucophage[®] family specifically dedicated to prediabetes.

¹ Chua, SJ, et al. Reprod Biol Endocrinol. 2021;19(1):1-13.

 $^{^{\}rm 2}\,{\rm B}\ddot{\rm u}hler$ et al. Reproductive Biology and Endocrinology 2021.

Concor[®] AM, our fixed dose combination drug of bisoprolol with amlodipine to treat hypertension, is now registered in 65 countries. In Q3 2021, we saw the launch in China where bisoprolol/amlodipine is the only long-acting single-pill combination (SPC) of a β -blocker combined with a calcium channel blocker. This is expected to fill the gap in B+C long-acting SPC treatment for patients in the country.

In 2021, the number of new patients using the Easypod[®] electromechanical injection device for treatment with Saizen[®] (somatropin) continued to grow, bringing the total number of patients enrolled on Easypod[®] Connect to around 25,000. Saizen[®] is our main endocrinology product and is indicated for the treatment of growth hormone deficiency in children and adults, while Easypod[®] Connect is a unique web-based platform that allows HCPs to monitor their patients' adherence to treatment with real-time injection data collected and transmitted from their Easypod[®] devices.

We continued the rollout of Aluetta[®], our new pen for the injection of Saizen[®], which complements our device portfolio and supports the growth of Saizen[®], taking the total number of countries where it is currently available to 28.

Building for the future

On July 6, we celebrated the topping out of the Biotech Development Center currently under construction in Corsier-sur-Vevey, Switzerland. This investment of \in 250 million, previously announced in January 2020, will help to sustainably secure capacity and high agility to deliver clinical trial material, contribute to accelerated development timelines of new biological entities, and address the increasing manufacturing complexity of the next generations of biotech compounds in a cost-effective way.

On July 19, we announced plans to invest \in 200 million at our global headquarters in Darmstadt by building a new Translational Science Center for the Healthcare business sector. As of 2025, the new Translational Science Center will offer room for more than 500 scientists, who will conduct research in a wide variety of fields ranging from the identification of disease biomarkers to the development of targeted therapies. This \in 200 million investment will give rise to an integrated, flexible-use laboratory building covering more than 30,000 m², that includes a lecture hall, in vitro laboratories including a cell bank, as well as a modern and flexible knowledge environment.

The Biotech Development Center and the Translational Science Center add to recent investments aiming to strengthen our capacities in the research, development, and manufacturing of medicines, notably at our R&D facility of Billerica, Massachusetts, United States, as well as at our biotech manufacturing site in Aubonne, Switzerland.

As of: December 31, 2021		
Therapeutic area		·
Compound	Indication	Status
Neurology		·
Evobrutinib (BTK inhibitor)	Relapsing multiple sclerosis	Phase III
Oncology		·
Tepotinib (MET kinase inhibitor)	Non-small cell lung cancer, METex14 skipping ¹	Registratio
Xevinapant (IAP inhibitor) Locally advanced squamous cell carcinoma of the head and neck ^{2,3}		
Berzosertib (ATR inhibitor)	Small-Cell Lung Cancer ⁴	Phase II
Tepotinib (MET kinase inhibitor)	Non-small cell lung cancer, EGFR mutant, MET amplified ⁵	Phase II
M1231 (Bispecific MUC1xEGFR ADC)	Solid tumors	Phase I
M1774 (ATR inhibitor)	Solid tumors ⁶	Phase I
M4076 (ATM inhibitor)	Solid tumors	Phase I
Peposertib (DNA-PK inhibitor)	Solid tumors ⁷	Phase I
Immuno-Oncology		
Avelumab (anti-PD-L1 mAb)	Non-small cell lung cancer, 1st line	Phase III
Bintrafusp alfa (TGFbeta trap / anti-PD-L1)	Cervical cancer 2nd line	Phase II
M6223 (anti-TIGIT mAb)	Solid tumors ⁸	Phase I
Immunology		
Enpatoran (TLR7 / 8 antagonist)	Systemic lupus erythematosus / Cutaneous lupus erythematosus	Phase I
Global Health		
Arpraziquantel (anthelmintic)	Pediatric schistosomiasis	Phase III
M5717 (PeEF2 inhibitor)	Malaria	Phase I

Additional information: Several combination studies (phase II) of avelumab with talazoparib, axitinib, ALK inhibitors or chemotherapy ongoing under sponsorship of Pfizer.

Unless noted otherwise, clinical programs conducted in collaboration with external partners are not shown unless we have co-ownership of data. More information on the ongoing clinical trials can be found at www.clinicaltrials.gov. Pipeline products are under clinical investigation and have not been proven to be safe and effective. There is no guarantee any product will be approved in the sought-after indication.

¹ As announced on December 17, 2021, the Committee for Medicinal Products for Human Use of the European Medicines Agency (EMA) adopted a positive opinion, recommending approval of tepotinib as monotherapy for the treatment of adult patients with advanced non-small cell lung cancer.

 $^{\rm 2}$ In combination with cisplatin and radiotherapy in unresected LA SCCHN patients eligible for cisplatin.

³ On March 01, 2021, we announced a worldwide in-licensing agreement with Debiopharm, Switzerland, for the development and commercialization of xevinapant (Debio 1143).

⁴ Includes studies (phase I/II) in collaboration with/ sponsored by external partners, e.g. US National Cancer Institute (NCI).

 $^{\rm 5}$ In combination with osimertinib.

 $^{\rm 6}$ Study as monotherapy and in combination with niraparib.

⁷ Study in combination with avelumab.

 $^{\rm 8}$ Includes study in combination with bintrafusp alfa.

1L: first-line treatment

2L: second-line treatment

ADC: Antibody Drug Conjugate

ATM: ATM serine/threonine kinase

ATR: Ataxia telangiectasia and Rad3-related protein

BTK: Bruton's tyrosine kinase

EGFR: Epidermal growth factor receptor

IAP: Inhibitor of Apoptosis Proteins

mAb: Monoclonal antibody

METex14: MET exon 14

MET: MET proto-oncogene, receptor tyrosine kinase

MUC1: Mucin 1, cell surface associated

PD-L1: Programmed cell death ligand 1

 $\label{eq:PeEF2: PeEF2: Plasmodium eukaryotic elongation factor 2$

PK: Protein kinase

TGFbeta: Transforming growth factor beta

Electronics*

Within our Electronics business sector, we are a technology leader and one of the leading players in most of our markets. As a science and technology company, we offer leading-edge products, services, and solutions that, in many cases, set us apart from the competition. Our business units are developing advanced materials for next-generation electronics. Our Chief Technology Office (CTO) is identifying trends and vetting technologies that are beyond the time horizon or scope of our business units. As a dedicated technology organization, the CTO is managing research partnerships, shaping our technology roadmaps, and managing our long-term R&D portfolio. We have also created a Technology Leadership Board to review and optimize our technology investment across the business sector.

In September, we announced our plans to invest significantly more than \in 3 billion in innovation and capacity until the end of 2025. These investments are an essential part of the new Level Up growth program. With this investment, we are also scaling up our research and development capabilities for next-generation semiconductor and display materials to further expand our position as a leading supplier to the electronics industry.

Semiconductor Solutions

We are addressing our customers' critical material needs through every step of the wafer manufacturing process. The outstanding capabilities and competencies of the businesses are diverse and will enable us to bring game-changing innovations for our customers into the market faster.

In Semiconductor Materials, our Thin Film Solutions business achieved significant progress in advancing critical PORs (Process of Record) for new organosilanes for conformal high-performance atomic layer deposition (ALD) and progressed our plasma-enhanced chemical vapor deposition (PECVD) for low dielectric constant applications. We continue to make progress in developing high-purity metal-containing precursor offerings enabled by new engineered container delivery systems. We also focus on developing new spin-on dielectric formulations for processes with improved dielectric characteristics for faster and better logic and memory devices.

With our Specialty Gases, we continue to make progress with our new etch gas technology program, which is focused on advancing the development of new chemistries to enable more than 100-layer single-stack etching for advanced memory devices such as V-NAND. We continue to see significant performance in new POR wins across our existing portfolio and new product introductions.

Our Patterning Solutions business continues to heavily invest in pattern transfer technologies for advanced nodes. The proliferation of extreme ultraviolet (EUV) lithography is gaining momentum in the industry, and our R&D programs for pattern collapse, underlayer, and image rectification are showing excellent progress at key customers. We are uniquely positioned to drive the implementation of organometallic compounds into the photolithography segment. We are seeing strong interactions in hard mask and resist development leading to improved performance. Additionally, advanced packaging technologies are driving innovation in conventional lithography materials. We are collaborating with the leading companies to support this innovation.

Our Silicon Valley-based material innovation accelerator Intermolecular saw an increase in the amount of work done in its labs for quantum computing and neuromorphic computing companies. These companies benefit from the flexible device processing infrastructure and deep materials knowledge to quickly achieve tangible products in these emerging technology areas. For more than 15 years, Intermolecular has been exploring, testing, and developing advanced materials that are revolutionizing the next generation of electronics.

Delivery Systems & Services (DS&S) develops, deploys, and operates the equipment that enables safe and reliable delivery of hazardous materials in semiconductor manufacturing. We are increasing the global

^{*} The contents of this chapter or section are voluntary and therefore not audited. However, our auditor has read the text critically.

manufacturing capacity of our state-of-the-art specialty gas, liquid chemical, and slurry delivery equipment to meet the growing demand in memory and foundry.

We released our CHEMGUARD[®] 600 model for bulk Tetrakis(dimethylamino)titanium (TDMAT) delivery, extending our TDMAT technology to remote, bulk supply to support our customers' ever-increasing flow rate and uptime requirements of advanced nodes. It also eliminates the need to use solvents to purge heat-sensitive, high-K precursors with low vapor pressures. The first container changes were completed and executed much faster than anticipated. It significantly reduces the container change time and provides a greener solution, surpassing our customer's performance expectations.

In addition, we have extended our GASGUARD[®] Active Control development to low vapor pressure compressed gases. Initially, it was developed to maintain, repeat, and stabilize pressure for high vapor pressure gases under varying manufacturing conditions and with zero pressure drift. GASGUARD Active Control now allows semiconductor fabs to achieve much greater precision in controlling the pressure of low vapor pressure compressed gases, such as Tungsten hexafluoride (WF₆) and others.

Most of the hazardous chemicals in liquid form are delivered by helium gas pressure to a wafer processing tool. We introduced CHEMKEEPER[®] GenX to reduce helium consumption by more than 50% of conventional systems.

At many customer sites, these technologies and other DS&S equipment are operated and maintained by our MEGASYS[®] Total Gas and Chemical Services team. As part of a global operations infrastructure, we are a premier supplier of semiconductor fab and sub-fab services to the worldwide electronics industry.

Display Solutions

Our display materials are enabling the fast-growing market of innovative displays for current and future applications such as foldable smartphones, rollable TVs, or AR/VR (Augmented Reality/Virtual Reality) devices. We further strengthened our ability to drive innovations in the attractive field of OLED displays by acquiring OLED patents from Konica Minolta in 2020. With liviFlex[™]-H, we are addressing challenges in the manufacturing of free-form OLED displays. Furthermore, we are active in the development of innovative material solutions for next generation displays, for example in the field of QD-PCC (Quantum Dot Pixel Color Converter), micro-LEDs, and AR/VR displays in close cooperation with customers and partners.

Our liquid crystal technology ultra-brightness fringe-field switching (UB-FFS) continues its successful growth, thanks to new product qualifications and rising demand in the liquid crystal displays (LCD) sector for mobile devices, especially mobile phones and tablet PCs. The development of high-resolution 4K and 8K TV sets continues to pose a challenge, as the LCD backlight transmission and efficiency will be reduced due to higher pixel density. We are therefore actively working to expand our ultra-bright (UB) technology offering with our UBplus liquid crystal materials for the TV market. With such technologies, we increase the light transmission efficiency of applications for large-format TV sets and display panels by 10% to 15%. This contributes hugely to the reduction of power consumption and helps our customers and consumers to meet sustainability targets.

Surface Solutions

In our Surface Solutions business, we focus on the empowerment of our customers to create surfaces that do what they need them to do – and look exactly the way they expect them to look. Thus, together with our customers we not only develop product innovations but more and more focus on new application technologies and process excellence to provide customized solutions for the individual challenges of our clients.

In our automotive pigments business, our pipeline consists of three pillars: product development, application engineering and effect visualization. We are actively working on the extension of our portfolio of Colorstream[®] multicolor effect pigments with outstanding saturation in the bluish red color space as an ideal complementation of the existing Colorstream[®] Lava Red. We will also add a fine light silver Iriodin[®] pigment to our metallic stylings offering a unique brightness and opacity.

With the development of a high viscous Durazane[®] polymer, we will extend the application field of anti-scratch and easy-to-clean coatings towards thicker films.

In addition, we push the boundaries of science and technology to lead our customers on the path to digitization of color evaluation processes. That is why we are implementing a digital setup that allows us to produce highly reliable color data as additional service for our customers.

In our Cosmetics business, we continue to put sustainability at the center of our efforts by more and more focusing on natural materials in our portfolio. Therefore, we will introduce additional cosmetic active materials from botanical sources with unique efficacy addressing anti-aging and anti-inflammatory claims. We also considered sustainability in the development of the first range of metal-free metal-look pigments for unique cosmetic effects based on proprietary and novel technology of pigment particle coating.

By broadening our portfolio of inorganic UV filters with two new products based on zinc peroxide (ZnO_2) , we will strengthen our position as one of the leading UV experts for light protection and tanning.

With the market introduction of additional specific specialties products for high-security applications, we will also extend our Securalic[®] portfolio offering our customers more reliable and highly discreet counterfeit detection.