



## Gyo Sagara

President,  
Representative Director,  
and CEO

# We are steering through the increasingly uncertain conditions with concrete strategies and steadfast determination to produce sustainable growth for the company and society.

### FY2021 Review

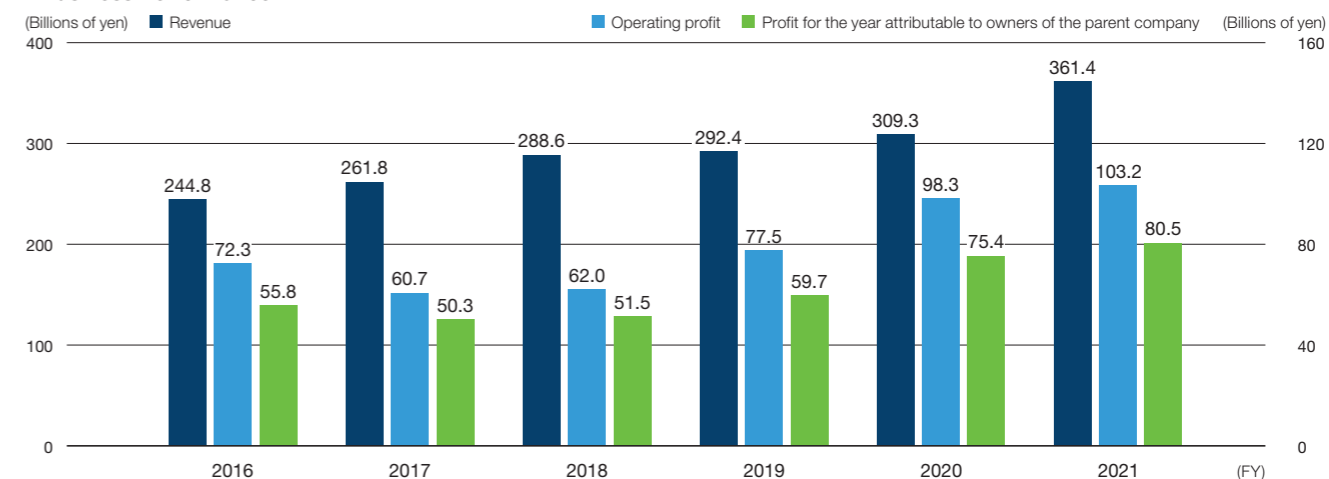
#### Steady progress with the growth strategy and a fourth consecutive year of growing sales and profits

The unsettled social conditions continued in fiscal 2021 as the ongoing coronavirus pandemic was joined by military conflict that rocked the global economy. Like companies around the world, the conditions deeply affected our business operations. Nevertheless, demand continued strong for our main products, including the OPDIVO intravenous infusion anticancer drug and FORXIGA Tablets for the treatment of diabetes and chronic heart failure and kidney disease. Our efforts during the year extended our business growth to four straight years with sales reaching 361.4 billion yen and operating profit 103.2 billion yen. I believe these results reflect the steady implementation of the four strategies we initiated in 2017 to establish a growth track through the long term. The strategies are designed to maximize product value, enhance our R&D capabilities, globalize our business, and strengthen our corporate infrastructure.

We took a significant step forward in fiscal 2021 with the first strategy of maximizing product value by winning approval of OPDIVO for first-line treatment of gastric cancer in Japan, South Korea, and Taiwan. OPDIVO was also approved in those countries as an adjuvant therapy for esophageal cancer, which increased the treatment lines. We also received approval for additional indications in Japan and South Korea, including for use of OPDIVO for as an adjuvant therapy for urothelial cancer.

We also made concrete progress advancing the other core strategies. We strengthened our R&D activities by initiating clinical trials for five new drug candidate compounds. We put more blocks in place to globalize our business by laying the groundwork for a direct sales system as we took another important step toward full-scale business operations in the United States. We are also strengthening our corporate foundation by enhancing our IT and digital infrastructure and cultivating talents to drive our globalization. These growth strategies produced strong results in fiscal 2021, and we will continue actively advancing them to maintain the momentum in our performance results.

### Business Performance



Industry Environment and Long-term Challenges

Aggressive R&D investment for further growth

The hurdles for new drug discovery in the pharmaceutical industry are extremely high. Some maladies, like hypertension and diabetes, have received much attention and many therapeutic agents employing various mechanisms of action have become available. However, effective therapies have proven elusive for many other ailments, notably cancer, diseases of the nervous system like Alzheimer's disease, and for still incurable infectious and immunological diseases. These are complicated diseases that will require highly targeted research to develop effective therapies, and their growing complexity means research will need more sophisticated technology, human resources, time, and cost while success becomes even more difficult to achieve. At the same time, the social conditions in Japan are making it increasingly difficult to recover R&D costs. Downward pressure on drug prices is growing as the government moves to counter the rising social security costs by controlling the costs of medicines and medical care. Lower prescription prices under the National Health Insurance system would reduce our revenue flow from existing products in Japan while constricting our ability to recover R&D costs when new products are released. Strengthening our drug development pipeline is essential to growing our business in these conditions. We do not have the expansive resources of a mega pharmaceuticals conglomerate. What we do have is the imagination and the ability to apply highly refined selectivity, plus the flexibility to fully incorporate open innovation. In the past, we have sought to maximize our resources by pursuing the research

principle that quality is the ideal, and quantity or scale is secondary. We now understand that a certain degree of scale is necessary to maintain a minimum standard of quality. Scale also helps accelerate product development. We are therefore revising our approach and are planning to allocate funds to be even more aggressive with R&D investment.

Even in the severe business environment, new methods are emerging that will help streamline and improve the efficiency of clinical trials at the development stage. One promising innovation comes from applying big data. Clinical trials are often conducted by comparing drug efficacy and safety from among two groups of participants, one group that takes the medicine being tested and a separate group that receives a placebo. We are learning how to use big data to mine information that will make the placebo group unnecessary, which has the potential to effectively cut the number of necessary clinical trial participants in half.

One impending issue is the patent cliff for our core OPDIVO product in 10 years. We were facing a similar situation when I was appointed president in 2008. At the time, 90% of the patents on our main products were due to expire within three or four years, and our research laboratories were not going to be able to produce new drugs in time to replace them. Our only choice was to look outside our organization and license drugs from outside. By mobilizing the whole company, we successfully licensed several drugs that provided a bridge until our own pipeline could reestablish our product flow.

The in-licensed new drugs we developed and launched held our sales steady until we gained real traction in 2014 with the approval of OPDIVO. Originally approved as a therapeutic agent for skin cancer, we have steadily developed and expanded its approval as a treatment for lung cancer, kidney cancer, and to 12 indications in total. Domestic sales of

OPDIVO amounted to 112.4 billion yen in fiscal 2021, and we expect domestic sales to reach 155 billion yen in fiscal 2022. In addition, we expect fiscal 2022 sales of our second biggest seller, FORXIGA, which in 2021 was also approved as an indication for chronic kidney disease, to reach 47 billion yen. With our sales continuing to grow each year, we plan to use the increasing cash flow for aggressive and effective investment and set a path for ongoing business growth.

Strategies for Sustainable Growth

Applying resources to licensing and in-house drug discovery to lead us to our long-term growth vision

In the current business environment, we believe that only companies that can maintain R&D investment above a certain threshold will continue to thrive. In recent years, our R&D investment has been near 70 billion yen annually. Comparatively, major Japanese pharmaceuticals companies spend over 200 billion yen and global mega pharmaceutical firms closer to 1 trillion yen. In the current conditions, we simply will not be competitive at our present level of R&D investment. There is no clear answer for how much investment will enable us to continue growing, innovating, and discovering new drugs; nor for what society will need from a pharmaceuticals company. The only sure way forward is through R&D, and we plan to incrementally raise annual R&D spending to 100 billion yen and then to 200 billion yen, matching the level of a leading Japanese

pharmaceuticals company. Aggressive R&D now is essential to extending our 300-year history another century.

The medium-term plan launched in 2017 was the first of three five-year plans that will guide our growth to 2031 when we plan to be investing 200 billion yen annually on R&D. The first R&D objective will be for the research laboratories to develop multiple new drugs that will be our next generation of products after OPDIVO.

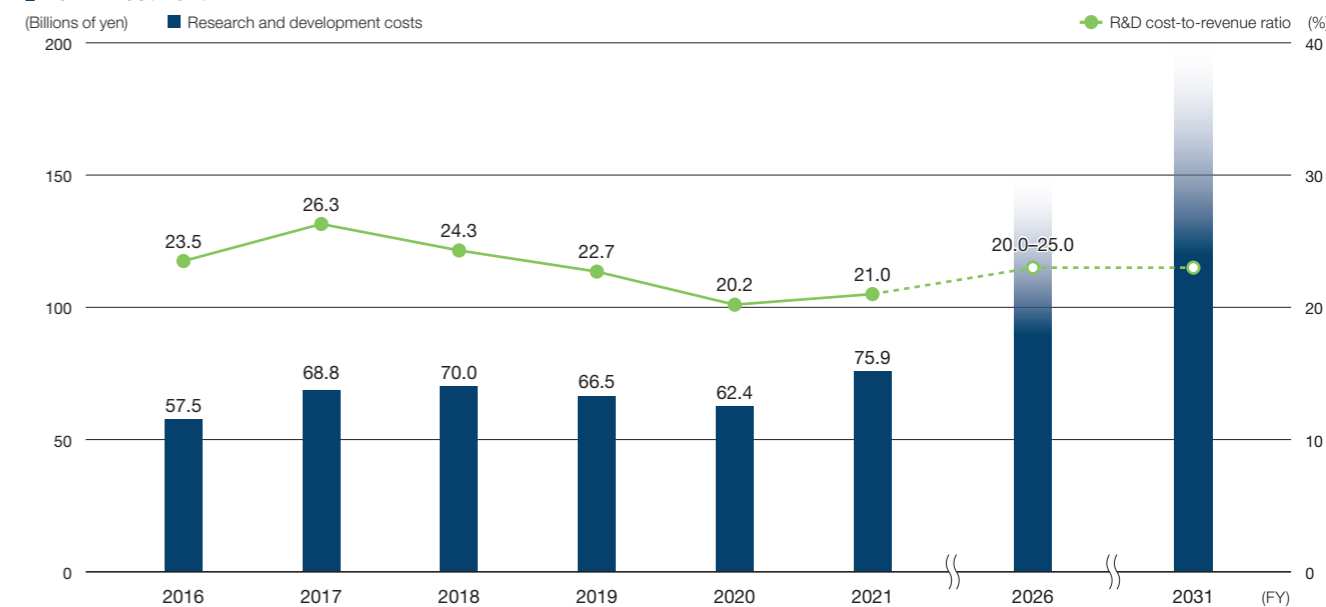
However, building up the development pipeline will take more than in-house drug discovery. We are therefore also actively engaging in joint research and drug discovery collaborations, stepping up our drug licensing activities, and seeking to broaden our coverage to markets beyond Japan and Asia.

The drug market in Europe is double and the United States market is five times the size of the Japan drug market. That means a product with sales of 30 billion yen in Japan has the potential for sales of 60 billion yen in Europe and 150 billion yen in the United States. In other words, a single successful product in those two major markets has the potential to generate 200 billion yen in sales. Imagine two products generating 400 billion yen, or three generating 600 billion yen. Although optimistic, these projections are significant considering that successful products in just those two markets could exceed the combined total sales and royalty income from OPDIVO in Japan, South Korea, and Taiwan.

That potential for that scale of sales revenue is why we are preparing to launch our own direct sales system in the United States and Europe. Extending our reach to those major markets from our focus on Japan will open opportunities for substantial growth.



R&D Investment





Identifying New Materiality Issues

Value creation and social contribution driven by our growth strategy and non-financial assets

We believe recognizing material issues not just for our CSR but also from a broader perspective will make us better able to advance our growth strategies, pursue wide-ranging value creation, and contribute to society. We have therefore combined our financial and non-financial issues into a single category of management materiality.

We are also focusing management assets on digital transformation and strengthening and cultivating our talents. Together, these are the foundation for the four growth strategies that we redefined in 2022: to maximize product value from the patient perspective, reinforce our pipelines and accelerate global development, establish direct sales system in the United States and Europe, and broaden our business domains.

In January 2022, we created the Digital & IT Strategy Division to serve as the IT headquarters for our enterprise

infrastructure. With the mandate to dramatically improve our management efficiency and innovation capabilities, the division will implement and support digital and IT systems that will dramatically improve work productivity and efficiency in the Discovery & Research, Clinical Development, CMC & Production, Sales and Marketing, and all departments.

Cultivating talents has always been a priority at Ono Pharmaceutical. Now more than ever, we need talented individuals who are highly skilled and motivated to pursue innovation for our growth strategies of new drug discovery and expansion into the global market. In May 2021, we created the Ono Innovation Platform to foster employee innovation capability and encourage all employees to take on new challenges and develop their talents as innovators. Another major theme is increasing the diversity of our staff. In the past, we followed a practice of building our ranks primarily with new college graduates. That served us well until about 10 years ago when we had the breakthrough with OPDIVO, our first oncology drug. Although we had experienced drug development staff and medical representatives (MRs) in the diabetes field, we knew it would take years to gain similar experience in the cancer field.

The solution was to open our hiring practices to bring in experienced mid-career professionals and then to bring in staff with wide-ranging expertise to accelerate development of the business.

We are now eagerly seeking to increase the diversity of our employees. In Japanese society, the first step to increasing diversity is to hire and promote the careers of women. We are also bringing in new employees with various backgrounds and personalities to stimulate innovation. We see the ultimate outcome of these initiatives as enhancing our ability to provide products that improve the lives of patients. If we can do that, we will generate the funds needed to continue advancing R&D and growing our business.

Diversity is also important to corporate governance. In 2020, the Board of Directors was invigorated by the appointment of our first female board member as an outside director. In 2022, we have taken it one step further by fortifying the external oversight and management expertise with the appointment of outside directors to serve as the chairs of the committees overseeing executive appointments and compensation.

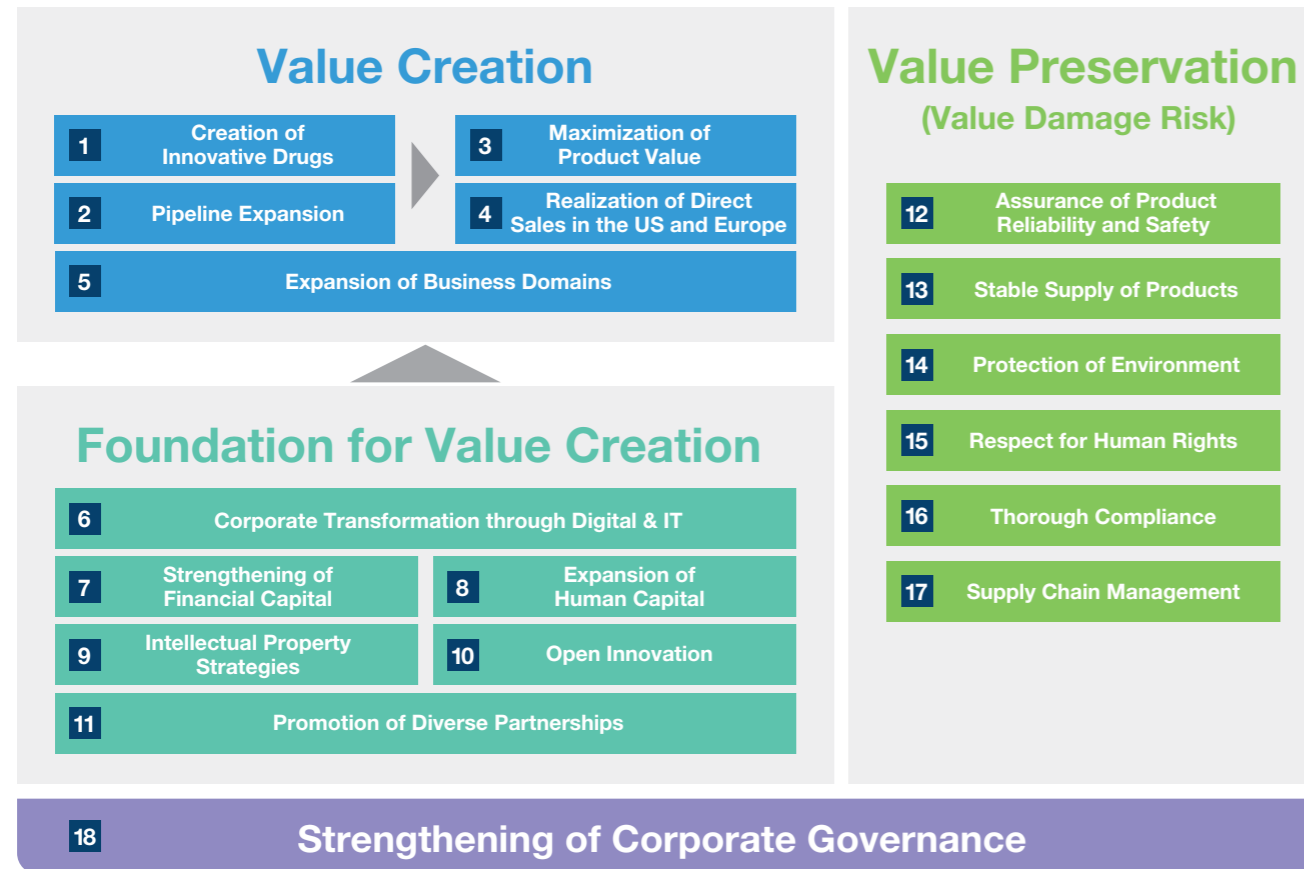
We are also establishing Ono Pharmaceutical as an environmental leader in the pharmaceutical industry by aiming to achieve high standards for environmental protection and seeking to do more than our part to protect the natural environment. We declared our support for the recommendations of the Task Force on Climate-related Financial Disclosures (TCFD) in October 2019, which we apply to our information disclosure and to the evaluation and management of risks and opportunities.

In June 2020, we became the first Japanese pharmaceutical company to join the RE100, an international initiative of businesses committed to using 100% renewable energy. As a company with a history going back three centuries, we believe we have a special obligation to actively participate in social movements, and we are stepping up our initiatives to contribute to the social good.



to discover and develop new drugs. The tasks for management and myself are to envision the direction forward, map out how to get there, and guide employees in the work that must be done. As president, I will be leading our efforts. Our jobs take up a large portion of the working day, and a fulfilling job is a cornerstone to a happy life. I intend to do everything in my power to make our company a place where every employee has the opportunity to take on challenges and grow. Ono Pharmaceutical has been a relatively small successful company for 300 years. We are now on the cusp of a major opportunity to grow. The opportunities may come at different times for different companies, and I want all of us to be ready to take the opportunity when it presents itself. Every mega pharmaceutical company started small. Our time to grow begins now. Our determination is strong, and we will make it happen. We would like to thank all our stakeholders for your continued support.

New Material Issues (Priority Management Issues)



Future Prospects and Aspirations

Major opportunity and strong determination

We want to be considered a vital element to a flourishing society. That is the fundamental goal of our business and our management and will be the source of our continuing success and growth. To achieve that, we will need to have a strong spirit of taking on challenges.

I envision a company where employees openly talk about their dreams because they know they have a chance to fulfill them. That spirit will be the driving force in our pursuit

*G. Sagara*