# Q&A | The 4th Medium-Term Management Plan Presentation (June 7, 2024)

| No | Questions | Answers |
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| 1 | Did you say that Otsuka will create products that contribute to solving social issues, based on the past experience that have made it easier for Otsuka to create such products, or that you would like to strengthen Otsuka's efforts and change its development policy in the future? If you change your policy, what do you think you will do in the 4th Medium-Term Management Plan (MTMP) period? | There has been no change in Otsuka's past and future policies regarding social issues. Looking back over the years since we went public, I am confident that Otsuka has been recognized as a company that is useful to society because we have created products that address social issues. For example, *ABILIFY* in the psychiatry and neurology areas, and *JYNARQUE* in the renal area became blockbusters. *JYNARQUE*, which was approved as *Samsca* with the concept of a diuretic that excretes only water, was approved for ADPKD (autosomal dominant polycystic kidney disease), for which there was no treatment. The FDA Advisory Committee pointed out the statistical analysis at the time of the approval review, and a phase 3 was redone. Subsequently, it was approved as an orphan drug for ADPKD in the US and became a major product. I believe that both *ABILIFY* and *JYNARQUE* have been highly recognized in the psychiatry and neurology and renal areas because we accomplished what only Otsuka could do.<br>In addition, we have successfully expanded the scope of our business from the past research and development (R&D) efforts in the past MTMPs, such as Taiho's R&D initiative using its unique cysteinomics drug discovery technology, its tie-up with Merck, and Astex's fragment drug discovery technology we gained through acquisition, and Pluvicto, which was initially developed as a diagnostic and has become a radioligand treatment for prostate cancer. In the 4th MTMP, we believe it is important to further enhance our R&D capabilities by incorporating necessary technologies from outside and forming new alliances. For example, the new Osaka Research Center for Drug Discovery is advancing immune-related research and drug discovery by analyzing the three-dimensional structure of proteins using cryo-electron microscopy. In this way, we are working to build a foundation to create innovation as an "innovation ecosystem" while incorporating various know-how and taking into account health needs.<br>We are aware that innovation comes from what we do not know will blossom, and that doing the same thing as other companies does not lead to innovation. For example, *POCARI SWEAT* was created with the idea of creating a beverage with an electrolyte composition similar to body fluids by utilizing the know-how of our intravenous solution business. It has gained global acceptance only because we provide data based on scientific evidence unique to a pharmaceutical company. Recently, heat stroke has become a problem in Japan as well as other countries, and children are sometimes rushed to hospitals for heat stroke at schools. So we are promoting not only our product but also heat stroke prevention measures needed due to social and environmental changes, which has opened up new opportunities for us.<br>The idea of identifying diseases that are troubling even if the number of patients is small, and needs that consumers are not yet aware of, and tackling them as social issues has not changed from the past, but I would like to broaden and deepen this approach in the future. I have given you a thorough explanation as this is the basic concept of our 4th MTMP. |

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| 2 | With respect to the concept of cash allocation, it is assumed that the impact of loss of exclusivity (LOE) of major products is large, but in reality, I think there may be a scenario where there is less LOE impact and an upside of business performance.<br>Therefore, please tell us your thinking on whether you have additional investment ideas in the case of higher performance, or whether a significant portion of the upside will be allocated to shareholder returns since you already have an efficient plan for R&D expenses. | As explained by Ms. Yuko Makino, Executive Director and CFO, on page 60 of the presentation material, the cash allocation for sustainable growth is 3 trillion yen in operating cash flow before R&D investment over 5 years. Of the cash allocation of 3.2 trillion yen, there is 1.5 trillion yen in R&D expenses, 500 billion yen for Pharmavite LLC in the US and capital investment in Asian countries, and 380 billion yen for conventional shareholder returns and share repurchases. Excluding these, there is approximately 800 billion yen in resources for acquiring external assets. It is necessary to allocate this considering how much to invest in the 4th MTMP period and how much the return will be in the 5th MTMP period.<br>At the stage where we can look ahead and get clearer picture on the situation, we believe that we will be able to tell a specific fund for shareholder returns. Therefore, one major theme of the 4th MTMP will be how to manage the ratio between investment and shareholder returns. |
| 3 | Regarding the peak sales shown in the reference materials on page 67, could you tell us about the upside potential of *Rexulti*?<br>I think the application acceptance and then approval by the FDA will lead to such an upside.<br>Given the success of *Rexulti*'s 061 Study and 071 Study, and the fact that there hasn't been a new drug approved in the US for over 20 years, and that MDMA-assisted therapy was not recommended for approval recently, I feel that *Rexulti* would be the only potential new treatment for PTSD.<br>Could you give us your feel for approval and the evidence supporting that feel? | An application for *Rexulti* for PTSD was filed in April. Despite the fact that 17 million people suffer from PTSD in the US, available treatment options are limited. We are aware of the FDA advisory committee's concerns about the safety of synthetic narcotics developed by other companies, as well as doubts about the effectiveness of the drugs demonstrated in comparison with placebo because of their clear hallucinogenic effects.<br>In the case of *Rexulti*, one phase 2 and one phase 3 results based on the strict study protocols are positive, so we think that *Rexulti* is eagerly awaited for approval and our expectations are high. The PTSD patient population is larger than that of AAD, which is approximately 2.8 million, so we believe the market is also large.<br>We hope that the additional indication will be approved and push up sales of *Rexulti*, further. |

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| 4 | The peak sales for sibeprenlimab, shown in the reference materials on page 67, is over 100 billion yen, but I think it is too modest. Based on the data presented by Vera, a competitor, there must be a larger number of patients with IgA nephropathy. Asahi Kasei Pharma acquired Calliditas Therapeutics, which owns Tarpeyo, a drug with the high cost of about 150,000 USD for 9 months. Sibeprenlimab is thought to be able to be used over the long term because it is an anti-APRIL antibody which suppresses the essential for treatment. Since the LOE is thought to be faraway in 2036, I believe that it is possible to estimate the sales well over 100 billion yen. Could you tell us about its potential upside? | REMS (Risk Evaluation and Mitigation Strategy) has been required for the current approved drugs for IgA nephropathy that do not target APRIL (A proliferation-inducing ligand). I cannot say for sure because the final decision will be made by the FDA, but sibeprenlimab might be evaluated favorably for its safety. As a unique point about safety, sibeprenlimab targets only APRIL and does not affect BAFF (B-cell activating factor). So it may be better that it does not to completely suppress IgM, IgG, and IgA production. One of the reasons for this assumption is that the rate of COVID-19 infection as an adverse effect was lower than that of placebo in the Phase 2 study we conducted during the COVID-19 pandemic. Although the detailed reason is unknown at present, we expect that it may be related to its safety characteristics. In addition, the monthly dosing interval may be an advantage. Although we cannot disclose the clear sales forecast at this time, we expect that sibeprenlimab will become the first choice as the development of various drugs with different MOAs increases the treatment options. |
| 5 | Has the progress of *Abilify MAINTENA* lawsuit changed? | As we are not at the stage where we can disclose this information, we will refrain from commenting on the litigation as it may involve other companies as well. |
| 6 | Regarding the oncology field on page 44, can you explain the reason why sales of *LONSURF* do not seem to be decreasing even in the 5th MTMP period as shown in the graph? | *LONSURF* has peripheral patents, but it is not disclosed how long they will be valid. In the oncology field, we would like to maximize the value by marketing products such as zipalertinib and ASTX030, which are expected to contribute to sales from the latter half of the 4th MTMP to the 5th MTMP. *LYTGOBI*, which was discovered by the cysteinomics drug discovery platform and has already been marketed, is under development for additional indications of esophageal and pancreatic cancers in the hope of generating synergistic effects when used in combination with other anti-cancer drugs. Zipalertinib is also in phase 1/2 for the second line and in phase 3 for the first line treatment of non-small cell lung cancer (NSCLC), respectively. |

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| 7 | Please tell us about the progress of life cycle management of LAI (long-acting injection) and once-weekly formulations of *Rexulti*. | Although it is difficult to develop LAI formulations for *Rexulti*, we will continue to explore various possibilities. The once-weekly formulation is being developed with the assumption that it will be launched in Japan. |
| 8 | The potential of centanafadine. In the US market, where stimulants are commonly used, its peak sales are reported to be over 100 billion yen. Can centanafadine succeed in the US market based on its safety features alone? | We believe that safety issues are important in the treatment of ADHD. Centanafadine shows clear efficacy and may be safer than existing non-stimulants. In particular, children with ADHD may suffer from insomnia, etc., when receiving medication, but centanafadine's unique formulation enables it to possess its unique pharmacokinetic profile of being effective only during the daytime. That should be a differentiating point of this asset. |
| 9 | Regarding anti-obesity drugs, the weight loss effect of drugs other than GLP-1 receptor agonists may be mild based on the recent clinical trial results of the products developed by other companies. Does NO-13065 result in mild weight loss compared to GLP-1 receptor agonists? What is the expected effect based on the mechanism? | NO-13065 is a drug with a novel mechanism of action (MOA). It acts on lipoprotein lipase in skeletal muscle, and the detailed MOA is currently being elucidated. Global phase 1b will commence in the future. NO-13065 has an MOA not related to appetite but related to energy consumption, and is considered to be a highly safe compound. It will take time to get to launch it, but we do have expectations for it. We hope it will become an exciting drug if its MOA is further clarified as we proceed with the clinical development. |

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| 10 | The company explained the foundation for innovation creation, business concept, and capabilities as the sources of growth on page 6. Please tell us where innovation creation originates and what leads to innovation. | We believe that corporate culture is important. Otsuka Pharmaceutical Co., Ltd., Otsuka Pharmaceutical Factory Ltd., Taiho Pharmaceutical Co., Ltd., and other pharmaceutical business core companies in the group have created their businesses with ingenuity and relentless exploration. This has become the basis of their corporate cultures which overlap the philosophy created by the founding families. We believe that a business requires a unique business concept, the ability of individuals and organizations to realize the concept, and the ability to demonstrate strength not only in Japan but also overseas. Our corporate culture is the foundation upon which these activities are carried out. We believe that a business can be realized when the company culture, its unique business concept, and the ability to realize it are all combined. We also believe that how employees learn about and pass on corporate culture is not only communicated verbally, but is passed on as a result of working together by management and employees. Otsuka currently has many projects, and we believe that the number of projects creates opportunities to pass on our corporate culture, which is good for the employees. We believe that it is the role of the management team to create as many opportunities as possible. |
| 11 | How does Otsuka incorporate the impact of the LOE of *Abilify MAINTENA*? Please tell us if you forecast it conservatively and you see an upside for royalty income and sibeprenlimab sales. | Regarding *Abilify MAINTENA*, we refrain from commenting because various negotiations are underway, including lawsuits. Regarding royalties, we would like you to ask our licensing partner companies, as it is up to their situation. We would like to do our best to expand sibeprenlimab opportunities by LCM strategy. |
| 12 | Please give us a breakdown of the revenue contribution of Next 8 products in terms of increase in revenue by 220 billion yen in FY2028 compared to FY2023. | Let me explain what impact each product will have in the 4th and 5th MTMP periods. Centanafadine, uRDN, sibeprenlimab, zipalertinib, INQOVI, and ASTX030 are expected to make substantial contributions during the 4th MTMP period. We are currently preparing for the ulotaront phase 3 program for schizophrenia again. Urotalont is expected to make a profit contribution during the 5th MTMP period, together with clinical study results for major depression and generalized anxiety disorder. *LYTGOBI* is also an asset with various opportunities, and is expected to make a profit contribution during the 5th MTMP period coming from expanding indications to other cancer types such as esophageal cancer. |