medigene

Q1 2022

MEDIGENE AG
QUARTERLY STATEMENT Q1 2022

PREAMBLE

For some time now, companies listed in the Prime Standard segment of the Frankfurt Stock Exchange have no longer been required to prepare full-length quarterly financial reports. Medigene takes advantage of this flexibility to focus attention on the key operational developments and key figures. This quarterly statement should be read in conjunction with the Annual Report 2021.

1 ABOUT MEDIGENE

Medigene AG (FSE: MDG1, ISIN DE000A1X3W00, Prime Standard) is a publicly listed biotechnology company headquartered in Planegg/Martinsried near Munich, Germany. With its scientific expertise, Medigene is working on the development of innovative immunotherapies to enhance T cell activity against solid cancers in fields of high unmet medical need.

Medigene's strategy is to develop its own therapies towards clinical proof-of-concept. In addition, the Company offers selected partners the opportunity to discover and develop therapies on the basis of its proprietary technology platforms. In return for such partnerships, Medigene expects to receive upfront and milestone payments as well as research and development funding and royalties on future product sales.

2 BUSINESS REVIEW SINCE THE BEGINNING OF 2022 AND OUTLOOK

2.1 T cell receptor-modified T cell (TCR-T) therapies

T cells are at the center of Medigene's therapeutic approaches. With the aid of Medigene's immunotherapies, the patient's own defense mechanisms are activated and T cells harnessed in the battle against cancer. Medigene's therapies arm the patient's own T cells with tumor-specific T cell receptors (TCRs). The resulting TCR-T cells should thereby be able to detect and efficiently kill cancer cells.

2.1.1 MDG1011 – clinically validated TCR-T therapy against PRAME in blood cancers

PRAME (PReferentially expressed Antigen in MElanoma) is meanwhile a quite well studied tumor antigen of the cancer-testis-antigen family which is over-expressed in various solid and blood cancers. Expression in healthy tissue is limited to the testis, which itself is an immune-privileged tissue that usually cannot be attacked by the body's own immune cells. This renders PRAME very suitable as a target antigen for TCR-T therapies.

MDG1011 is Medigene's first proprietary TCR-T immunotherapy candidate directed against PRAME that entered clinical development. In a multicenter, open-label Phase I/II study, MDG1011 is being evaluated in blood cancer patients suffering from advanced-stage acute myeloid leukemia (AML), myelodysplastic syndrome (MDS) or multiple myeloma (MM).

In the Phase I portion (3+3 dose-escalation part), patients received MDG1011 as a single intravenous infusion at fixed dose levels of 0.1, 1, or 5 million TCR-T cells per kg body weight, following standard pre-conditioning. The primary study objectives were to evaluate the safety, tolerability, and feasibility of manufacturing MDG1011

TCR-T cells. In addition, preliminary signs of clinical efficacy and immune monitoring data were examined, along with other secondary study objectives.

In June 2021, the last patient was enrolled in the third dose cohort and Medigene reported on safety, tolerability and feasibility in December 2021. In February 2022, first efficacy and immune monitoring data were published.

MDG1011 was successfully produced for 12 of the 13 heavily pretreated patients (92.3%). Four patients succumbed to their disease before treatment could be administered, which was consistent with the severity of the study patients' underlying disease. Therefore, nine patients received MDG1011 in the Phase I portion of the study.

Overall, MDG1011 proved to be safe and well tolerated. All patients experienced manageable adverse events, with a preponderance of treatment emergent adverse events (TEAEs) expected for the underlying cancer. Two patients experienced grade 1 or 2 transient cytokine release syndrome (CRS) attributable to MDG1011. This is direct evidence of the biological activity of the infused T cells. No immune effector cell-associated neurotoxicity syndrome (ICANS) was observed, nor were any dose-limiting toxicities (DLT) reported.

One MDS patient treated at the highest dose level remained without detectable progression to secondary AML nine months after MDG1011 administration and continues to be under observation. Another patient treated at the lowest dose level experienced complete remission in the fourth week after treatment; however, this clinical response was not durable and the disease continued to progress at eight weeks.

Immune monitoring of patients included detection of PRAME-specific T cells (MDG1011 TCR-T cells) in blood to determine their persistence over time and biomarker tracking of PRAME in bone marrow and/or blood as an indicator of remaining cancer cells. The resulting data supported the clinical efficacy and biological activity outcomes.

In line with Medigene’s focus on solid cancers, the Company has decided that, contingent on the final results from the Phase I part, the Phase II part of the trial would only be conducted with or by a partner.

2.1.2 Unique tumor-specific antigens (TSAs) – the “dark matter” of our genome

In January 2020, Medigene entered into a research collaboration focusing on novel cancer antigens for highly specific immunotherapies with the University of Montréal and IRICoR, a pan-Canadian drug discovery research commercialization center. The collaboration was expanded in December 2021.

Under the collaboration agreement, Medigene has gained access to 47 potential tumor-specific antigens (TSAs). These peptides were found to be shared among specimens of several patients with solid tumors of different origin, such as ovarian, breast, and lung cancer, but were not detected in healthy tissues. This characterizes them as TSAs and renders them highly interesting for development of future effective and safe cancer immunotherapies.

Ten TSAs proved to be immunogenic and thus able to induce specific T cell responses. To date, Medigene has isolated more than 20 TCRs of T cell clones that recognize these novel TSAs and have the potential to become next-generation TCR-T therapy candidates. Their further functional and safety characterization is ongoing.

2.2 Tools to empower TCR-T therapies

In addition to optimizing the identification and characterization of new TCRs, Medigene is developing numerous innovative tools to make TCR-T therapies even safer, more specific and more effective, especially for use in solid cancers. Research is also continuously being conducted into how TCR-T cells could be maintained in patients for longer, and to make the manufacturing process of TCR-T cells faster, more efficient and more cost-effective.

2.2.1 PD1-41BB switch receptor - persistence of function

The PD1-41BB switch receptor is the most advanced of the TCR-T enhancement technologies currently being developed by Medigene. Solid tumors can avoid immune control by utilizing a number of mechanisms to hide from the immune system and evade T cells or to actively suppress T cell attack. Such mechanisms include the expression of the checkpoint molecule PD-L1 on the tumor cell surface. PD-L1 interacts with its PD-1 counterpart on T cells and delivers a signal that turns off T cell function. Medigene's PD1-41BB switch receptor is expressed on TCR-T cells and the off-signal sent to the TCR-T cells by PD-L1 on tumor cells is directly converted into an activation signal instead.

A current approach in the field to avoid inhibition of TCR-T cells by PD-L1 is to use a combination therapy of TCR-T cells and a checkpoint inhibitor antibody that interferes with the PD1-PD-L1 axis. With our approach, combination therapies are not needed and increased side effects and higher therapy costs could be avoided.

Preclinical experiments have already demonstrated that the addition of the PD1-41BB switch receptor enhances both the effector functions of TCR-T cells and their ability to eradicate PD-L1-positive solid tumors. The data were published in March 2022 in the peer-reviewed scientific publication "T-Cells Expressing a Highly Potent PRAME-Specific T-Cell Receptor in Combination with a Chimeric PD1-41BB Co-Stimulatory Receptor Show a Favorable Preclinical Safety Profile and Strong Anti-Tumor Reactivity" in the scientific journal *Cancers*.

In February 2022, Medigene granted BioNTech SE (BioNTech) a license to the PD1-41BB switch receptor. For further details on this partnership, please refer to section 2.3.1.

2.2.2 Precision pairing library

TCRs consist of an alpha and a beta chain that sit together as one receptor on the cell surface of T cells. Medigene's precision pairing library is designed to improve the functionality and safety of TCR-T cells. This is done by increasing the number of TCRs on the cell surface and/or by ensuring that the TCR-T cells carry only the intended, newly introduced TCR on their surface, but not arbitrary combinations of single chains of the new TCR and the TCR already contained in the recipient T cell.

In February 2022, Medigene granted BioNTech a license to the precision pairing library. For further details on this partnership, please refer to section 2.3.1.

2.2.3 iM-TCR

Medigene has developed the inducible Medigene TCR (iM-TCR), a technology to improve the safety of TCR-T therapies. iM-TCRs are modified so that full control of TCR surface expression can be achieved and thereby activity against tumor cells can be fine-tuned such that potential unwanted toxicity against normal cells can be controlled if needed. This property would be of great interest in brain or liver cancer, for example, as these organs could be damaged by a persistent inflammatory T cell response.

TCRs containing the iM-TCR signature only appear on the surface of TCR-T cells when the patient is given tamoxifen, a comparatively affordable, well-established and well-characterized drug that has been approved for years.

Preclinical experiments have already shown that the iM-TCR system only forms correctly paired TCRs and does not mis-pair with other TCR single chains originally present in TCR-T cells, and that iM-TCR-expressing T cells are tightly controlled by the dose and timing of tamoxifen-induced expression. In the future, this would allow physicians to finely regulate TCR-T activity or even turn it on and off as needed.

2.2.4 Dendritic cell (DC) technology

Dendritic cells (DCs) are an essential component of Medigene's platform for identifying and characterizing future TCR candidates. DCs serve as antigen-presenting cells to activate T cells that specifically recognize a selected target antigen.

In addition to the continuous use of DCs in the high-throughput TCR discovery process, Medigene has developed and clinically evaluated a new generation of vaccines based on antigen-tailored DCs. The positive results of the completed open-label Phase I/II trial in AML patients were confirmed even after more than 3.5 years of median follow-up, as reported in February 2021. The data indicate that patients who received the DC vaccine could potentially have persistent clinical benefit without experiencing serious adverse events (SAEs) associated with treatment.

However, as Medigene's development focus is on TCR-T therapies, DC vaccines per se as a stand-alone therapy will only continue in the context of partnerships such as the one in place for the Asian region with Roivant/ Cytovant. Recently, a competing product has been approved as maintenance therapy for patients with AML in the U.S. and Europe, and Medigene expects similar approvals to be granted in other regions, including China, in the near future. These current events affect the development of the DC vaccine under the existing partnership as well as Medigene's further partnering endeavors.

In Medigene's clinical trials of MDG1011 TCR-T cells and of the DC vaccine in blood cancers, the manufacturing processes needed to make patient-specific TCR-T cells or DCs from patients' leukapheresis material was established for both cell types. Both manufacturing processes obtained regulatory approval to be applied in the respective trials and the feasibility of manufacturing cellular products of high quality was established in the two clinical studies.

Medigene is currently investigating whether TCR-T therapies and DC vaccines could potentially be combined in the future to ensure that TCR-T cells are maintained and proliferate in patients for longer periods of time through DC vaccine boosters. The fact that both cell products could be manufactured from the same starting leukapheresis material would simplify the development of such a combination therapy.

2.3 Development partnerships

In addition to the discovery and development of TCRs and tools to further improve T cell-based immunotherapies in the future for its own product pipeline, out-licensing and partnerships with other companies form a second, very important pillar for Medigene. When concluding a new partnership, Medigene usually receives an upfront payment of several million euros. In the further course of the partnerships, Medigene is reimbursed for the research and development expenses incurred for the respective projects and potentially receives future milestone payments and royalties for products based on Medigene's discoveries and technologies.

2.3.1 New comprehensive TCR-T and technology partnership with BioNTech

In February 2022, Medigene and BioNTech signed a global strategic partnership to advance TCR-based immunotherapies against cancer. Under the terms of the agreement, Medigene has received a payment of €26 m and will be reimbursed for the research and development costs incurred for the period of the collaboration. The research collaboration will encompass several target structures and has an initial term of three years. Medigene will contribute its proprietary TCR discovery platform for the development of TCRs against multiple solid tumor targets nominated by BioNTech. BioNTech will be responsible for global development and hold exclusive worldwide commercialization rights on all TCR therapies resulting from this research collaboration.

BioNTech acquired Medigene's TCR-4 of the MDG10XX program targeting the cancer antigen PRAME. BioNTech also obtained the exclusive option to acquire additional existing TCRs in Medigene's discovery pipeline and received licenses to Medigene's PD1-41BB switch receptor and precision pairing library. This has the potential to augment TCR cell therapy efficacy and can be applied to all BioNTech cell therapy programs.

Medigene will be eligible to receive development, regulatory and commercial milestone payments up to a triple digit million Euro amount per program in addition to tiered deferred option payments on global net sales for products based on TCRs arising from the collaboration and royalties on products utilizing at least one of the licensed technologies.

2.3.2 TCR-T partnership with 2seventy bio (formerly: bluebird bio)

In 2016, Medigene and bluebird bio, Inc. (bluebird bio) entered into a strategic research and development collaboration and licensing agreement encompassing TCR immunotherapies against four targets. This agreement was expanded in 2018 to six targets. In November 2021, bluebird bio spun off its oncology business into the newly formed company 2seventy bio, Inc. (2seventy bio) and all contracts concluded with Medigene were transferred to 2seventy bio.

The most advanced project in the collaboration is a TCR specific for a peptide stemming from the MAGE-A4 protein, a tumor antigen from the cancer-testis antigen family. This TCR is different to other MAGE-A4-specific TCRs in development elsewhere as it works independently of signaling through the co-receptor CD8, which is found on so-called killer T cells. In this way, any helper T cells (which express CD4 and not CD8), equipped with Medigene's MAGE-A4 TCR can also detect and kill cancer cells presenting the MAGE-A4 antigen on their surface.

The research work describing the selection and activity of this TCR has been published recently in the Journal for ImmunoTherapy of Cancer and received the "Best Immune Cell Therapies and Immune Cell Engineering Paper Award" from the Society for Immunotherapy of Cancer (SITC) in 2021.

2.3.3 TCR-T and DC partnering with Roivant/Cytovant

In 2019, Medigene entered into license and cooperation agreements with Cytovant Sciences HK Limited, a biopharmaceutical company founded by Roivant Sciences (Roivant/Cytovant), which cover a TCR that is directed against the tumor antigen NY-ESO-1, two TCR-T development projects as well as Medigene's DC vaccine, for Asia including the People's Republic of China, Hong Kong, Macao, Taiwan, South Korea, and Japan. Roivant/ Cytovant on the one hand reported that their development activities would be delayed due to the COVID-19 pandemic, and on the other hand has temporarily suspended Medigene's TCR discovery activities within the second TCR-T development project since April 2022.

2.4 Change in the Executive Management Board

At the end of March 2022, Axel Malkomes, former Chief Financial Officer and Chief Business Development Officer (CFO&CBO), left the Company's Executive Management Board by mutual consent at the expiry of his contract. Since then, Dr. Birger Kohlert acts as CFO, who was Vice President Finance, Controlling, Procurement and IT at Medigene since January 2020. Dr. Kohlert looks back on years of international experience in finance and was previously CFO at S + P Samson, Kissing, Germany, EvoBus Sweden and EvoBus Denmark. Prior to that, he had several positions in the finance department of the Daimler Group in Germany and the USA and in the audit department of KPMG in Germany. He holds a doctorate in the field of international accounting.

3 FINANCIAL DEVELOPMENT AND FORECAST

Total revenue in Q1 2022, Medigene generated revenue of €23,023 k compared to €2,146 k in Q1 2021. This increase in revenue mainly results from revenue recognized from components of the new partnership with BioNTech concluded in February 2022. Revenue in Q1 2022 also includes revenue from the derecognition of contract liabilities and from research and development services.

Research and development expenses of €2,017 k in Q1 2022 were €1,995 k less than in the prior-year quarter (Q1 2021: €4,012 k) which is still due to the focus on TCR-T therapies for the treatment of solid tumors. As a result, the earnings before interest, taxes, depreciation, and amortization (EBITDA) increased by €19,854 k on the prior-year quarter (Q1 2021: €-3,078 k), amounting to €16,776 k in Q1 2022.

Medigene confirms its financial forecast for 2022 published in the Group Management's Discussion and Analysis 2021, which reflects the Company's focus on and progress in the core business of immunotherapies. These estimates do not include potential future milestone payments from existing or future partnerships or transactions, as the occurrence of such events or their timing and extent largely depend on external parties and therefore cannot be reliably predicted by Medigene. The Company continues to expect revenues of €23 – 28 m, research and development expenses of €11 – 15 m and a positive EBITDA in the amount of €3 – 5 m in 2022.

Currently, Medigene does not expect any material impact due to COVID-19 or the Ukraine crisis on revenues, research and development expenses and EBITDA.

As of 31 March 2022, cash and cash equivalents amounted to €47,808 k (31 December 2021: €22,417 k). The increase in total cash and cash equivalents in Q1 2022 compared to the end of 2021 is primarily due to the payment of €26 million received under the new partnership with BioNTech less Medigene's research and development expenses to advance Medigene's clinical and preclinical activities in Q1 2022. Based on its current planning, the Company has sufficient financial resources to fund business operations into Q4 2024.

4 OPPORTUNITIES AND RISKS

For a detailed description of the opportunities and risks associated with the Company's business activities as well as the risk management and internal control system, please refer to Section 4 of the Group Management Report in the Annual Report 2021, as these have remained largely unchanged since the approval of the 2021 Consolidated Financial Statements on 15 March 2022. The occurrence of any one of the risks described in the Group Management's Discussion and Analysis – alone or in conjunction with each other – could have a negative impact on the results of operations, financial position and net assets of Medigene.

Financial calendar 2022

Quarterly Statement Q1 2022	4 May 2022
Annual General Meeting 2022	18 May 2022
6-Months Report 2022	3 August 2022
Quarterly Statement Q3 2022	2 November 2022

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