medigene

Q3 2022

MEDIGENE AG
QUARTERLY STATEMENT Q3 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 as well as the 6-Months Report 2022.

1 ABOUT MEDIGENE

Medigene (FSE: MDG1) is a late pre-clinical stage immuno-oncology company, focusing on discovering and developing differentiated, breakthrough cellular therapies to improve the lives of cancer patients. With an end-to-end technology platform built on multiple proprietary and exclusive product enhancement and product development technologies, Medigene aims to create best-in-class T cell receptor-modified T cell (TCR-T) therapies that are optimized for both safety and efficacy. Medigene's strategy is to develop product candidates both for its in-house therapeutics pipeline and for partnering.

2 BUSINESS REVIEW SINCE THE BEGINNING OF 2022 AND OUTLOOK

T cells are at the center of Medigene's therapeutic approaches. With the aid of Medigene's immunotherapies, the patient's own immune system is 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) and the resulting TCR-T cells are designed to detect and kill cancer cells. Medigene's end-to-end technology platform aims to optimize the development of these TCR-T therapies as well as to enhance their potential safety and efficacy to treat cancer.

2.1 Target antigen screening – Improving safety and efficacy

Medigene continuously evaluates new potential cancer target antigens for future TCR development, both using its in-house technologies and through external collaborations with leading academic institutions. These antigens must fulfill clear criteria such as significant immunogenicity, a lack of cross-reactivity with healthy tissue as well as clinical and commercial relevance.

Medigene's EXPItope-M technology is a proprietary, self-updating library using advanced analytics of multiple databases that can predict and identify immunogenic fragments of proteins, so-called "epitopes", for potential TCR production and that addresses the challenges seen where not all epitopes either bind to the designated presenting molecule, the human leukocyte antigen (HLA), or are produced in the cell. This allows Medigene to identify epitopes suitable for TCR production that have low potential for cross-reactivity to off-target tissues with the potential for improved safety and can also predict binding affinities to support great efficacy.

Through its research collaboration with the University of Montréal and IRICoR, a pan-Canadian drug discovery research commercialization center, Medigene investigated a set of 47 novel tumor-specific antigens (TSAs) through its proprietary, bioinformatics-driven high-throughput screening tools. Fifteen TSAs proved to be immunogenic and thus able to induce specific T cell responses. In particular, all of the TSAs we have studied were found to be expressed distinctively in ovarian cancer only. However, none passed Medigene's high-set

criteria for the selection of target antigens suitable for the clinical development of TCR T cell therapy in a wider range of cancers. Therefore, Medigene will not further pursue the analysis and characterization of these potential targets but focus its resources on target antigens which are deemed more promising for the development of T cell-based adoptive cell therapies.

2.2 TCR discovery engine – Developing TCR-T therapies through optimal sensitivity, specificity and safety

Using Medigene's TCR discovery process, the Company continuously discovers and characterizes new TCRs against various target antigens for the Company's own development pipeline or for potential partnering.

Medigene's process starts by sourcing blood or tissue samples from multiple healthy donors who have not been exposed to the inhibitory effects of having cancer and deleterious cancer treatments, and who therefore have a fully functioning immune system that will allow them to respond well to the Company's selected target antigens.

Using its proprietary allo-TCR priming technology, Medigene generates enriched T-cells primed with the target antigen resulting in thousands of individual T cell clones. These clones are analyzed by high-throughput screening and those with defined response characteristics are selected and a collection of unique TCRs is then built through iterative rounds of priming with multiple additional healthy donors until there are up to several dozen TCR sequences to vet against each other to find the lead TCR with an optimal specificity, sensitivity and safety profile.

Through this process, Medigene has created optimized TCRs such as its first clinically evaluated PRAME-specific MDG1011 TCR (see section 2.3), the CD8 co-receptor independent MAGE-A4-specific TCR delivered to 2seventy bio, Inc. (2seventy bio), the PRAME-specific TCR-4 acquired by BioNTech SE (BioNTech) and the NY-ESO-1-specific TCR out-licensed for Asia to Hongsheng Sciences HK Limited (Hongsheng Sciences). For more information on Medigene's partnerships please refer to section 2.6.

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

PRAME (PReferentially expressed Antigen in MElanoma) is a well-studied tumor antigen of the cancer-testis-antigen family which is over-expressed in various solid and blood cancers, whilst limited in healthy tissue 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 more than a year after MDG1011 administration and remains under observation in a long-term follow-up study linked to the now concluded Phase I study. 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 eight weeks later.

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.

2.4 TCR-T therapy product enhancement and development optimization technologies

In addition to the identification and characterization of new TCRs and target antigens, 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. A selection of these is described below.

2.4.1 PD1-41BB switch receptor – Persistence of function

The PD1-41BB switch receptor is the most advanced of the TCR-T enhancement technologies currently being used by Medigene.

Solid tumors can create a hostile tumor micro-environment that significantly diminishes the ability of T cells to kill tumor cells, by enabling these tumor cells to evade T cells or to actively suppress a 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 Medigene's approach, combination therapies are not needed and increased side effects and higher therapy costs could be avoided. Using the Company's single tool can lead to therapeutic improvements on multiple levels such as enhanced T cell functionality, *in vivo* T cell persistence, sustained T cell proliferation and reduced T cell exhaustion.

Preclinical data underlining these potential effects 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 2.6.1.

2.4.2 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 ensuring that the TCR-T cells carry only the intended, newly introduced recombinant TCR on their surface, but not arbitrary combinations of single chains of the new recombinant TCR and the endogenous TCR already contained in the recipient T cell, thus avoiding a mismatch and potential for off-target undesired adverse effects and also helping to improve TCR-T functional activity.

In February 2022, Medigene granted BioNTech a license to the precision pairing library. For further details on this partnership, please refer to section 2.6.1.

2.4.3 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.

2.5 Other technologies – Dendritic cell (DC) vaccines

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.

2.6 Development partnerships

Out-licensing and partnerships with other innovative immuno-oncology companies forms an important value creation pillar for Medigene, in addition to Medigene’s wholly owned pipeline of TCR-T therapies. A partnership may generate revenues for Medigene in the form of upfront payments, potential for reimbursement of expenses incurred by Medigene for the continuation of research and development required by the partner, and from potential future milestone payments as well as royalties based on commercial sales for products based on Medigene’s TCRs, TCR-T therapies or innovative tools from its end-to-end technology platform.

2.6.1 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 two of Medigene’s key product enhancement technologies from its technology platform, the PD1-41BB switch receptor and the precision pairing library, which have the potential to augment TCR cell therapy efficacy and can be applied to all BioNTech cell therapy programs.

Medigene will also be eligible to receive future 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.

The acquisition of the TCR targeting PRAME and the licensing of the two key technologies, are a further validation of Medigene’s scientific leadership and the value inherent in its end-to-end technology platform.

2.6.2 TCR-T partnership with 2seventy 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 and all contracts concluded with Medigene were transferred to 2seventy bio. At the end of June 2022, the research term for this partnership was concluded in accordance with the contract. Medigene remains eligible for milestone payments and royalties from 2seventy bio as per the existing agreement.

The most advanced project in the collaboration is a highly differentiated 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 being developed by other companies as it works independently of signaling through the co-receptor CD8, which is found on 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.

2.6.3 TCR-T and DC partnering with Hongsheng Sciences

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 additional 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).

Medigene was informed that Roivant Sciences divested its holding in Cytovant Sciences in July 2022, which subsequently became Hongsheng Sciences. Due to financing constraints, Hongsheng Sciences has temporarily suspended its development activities within the Medigene partnership.

2.7 Changes in the Executive Management Board

Medigene's Supervisory Board has appointed Dr. Selwyn Ho as a member of the Executive Management Board effective 25 July 2022 and appointed him as the new Chief Executive Officer (CEO). As a consequence, Prof. Dolores Schendel stepped down as Chief Executive Officer at the end of 24 July 2022 and now fully focuses on her responsibilities as Chief Scientific Officer (CSO) and Head of Research and Development at Medigene.

Dr. Ho received his medical degree (MB BS) and Bachelor of Science (BSc) in Pharmacology from Imperial College, University of London, UK, and post-graduate qualifications (Dip Pharm Med) in Pharmaceutical Medicine from the Faculty of Pharmaceutical Physicians, Royal College of Physicians, UK. In addition to his medical and pharmaceutical background, he has over 20 years of international experience across Europe, US, and Asia in executive and senior management positions in both privately held and publicly traded biotech and pharma companies with a focus on inflammation and immunology, with various responsibilities in the areas of Product Development, Medical Affairs, Strategic Marketing and Market Access, Business Development and Licensing as well as Corporate Strategy and Financing.

Dr. Ho joins Medigene from Connect Biopharma (NASDAQ: CNTB), a global clinical-stage biopharmaceutical company developing therapies against chronic inflammatory diseases derived from T cell-driven research, where he held the position of Chief Business Officer and, amongst other responsibilities, jointly led the execution of the company initial public offering (IPO) which closed in March 2021. Dr. Ho also serves as an Executive-In-Residence at New Rhein Healthcare Investors, a venture capital and growth stage fund focused on healthcare therapeutics and medical devices and is a Non-Executive Director for Immodulon Therapeutics Ltd., a clinical stage company developing novel therapies for cancer based on bacterial derived immunomodulators.

Since the end of March 2022, Axel Malkomes, former Chief Financial Officer and Chief Business Development Officer (CFO&CBO), has left the Company's Executive Management Board by mutual consent at the expiry of his contract. Since then, Dr. Birger Kohlert acts as CFO, and has been Vice President Finance, Controlling, Procurement and IT at Medigene since January 2020. Dr. Kohlert has more than 20 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

In Q3 2022, Medigene generated revenue of €1,424 k compared to €2,187 k in Q3 2021. This decline in revenues was mainly due to the suspension of activities within the partnership with Hongsheng Sciences. Revenue in Q3 2022 also includes revenue from the derecognition of contract liabilities and from research and development services for the partnerships with 2seventy bio and Hongsheng Sciences.

Research and development expenses of €3,258 k in Q3 2022 were €766 k higher than in the prior-year quarter (Q3 2021: €2,492 k) which is due to additional charge of costs for the MDG1011 clinical trial. As a result, the earnings before interest, taxes, depreciation, and amortization (EBITDA) decreased by €2,009 k versus the prior-year quarter (Q3 2021: €-1,754 k), amounting to €-3,763 k in Q3 2022.

In November, Medigene adjusted its financial forecast for 2022 previously published in the Group Management's Discussion and Analysis 2021 due to the successful closing of the MDG1011 clinical trial as well as further savings. 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 expects revenues of €23 – 28 m, research and development expenses of €9 – 11 m and a positive EBITDA in the amount of €8 – 9 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 30 September 2022, cash and cash equivalents including time deposits amounted to €35,978 k (31 December 2021: €22,417 k). The increase in total cash and cash equivalents in the first three quarters of 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 the first three quarters of 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.

Imprint

Date of publication

2 November 2022

Published by

Medigene AG
Lochhamer Str. 11
82152 Planegg/Martinsried
T +49 (0) 89 2000 330
F +49 (0) 89 2000 3329 20

Contact

Investor Relations & Corporate Communications
T +49 89 2000 3333 01
investor@medigene.com

Trademarks

Disclaimer

This text contains forward-looking statements that are based on certain assumptions and expectations made by the management of Medigene AG at the time of its publication. These forward-looking statements are therefore subject to unpredictable risks and uncertainties, so there is no guarantee that these assumptions and expectations will turn out to be accurate. Many of those risks and uncertainties are determined by factors that are beyond the control of Medigene AG and cannot be gauged with any certainty at this point in time. This includes future market conditions and economic developments, the behavior of other market participants, the achievement of targeted synergy effects as well as legal and political decisions. Medigene AG cannot preclude that actual results may differ substantially from those expectations expressed in or implied by the forward-looking statements. Medigene AG does not intend or assume any obligation to update any forward-looking statements to reflect events or circumstances after the date of this text.

The English version of the text is a translation of the original German version; in the event of variances, the German version shall take precedence over the English translation.

LIVING IMMUNOTHERAPIES

WWW.MEDIGENE.COM