medigene

# Q3 2021

MEDIGENE AG
QUARTERLY STATEMENT Q3 2021

# 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 2020 as well as the 6-Months 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 pipeline includes preclinical as well as clinical programs in development.

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 2021 AND OUTLOOK

## 2.1 T cell receptor-modified T cell (TCR-T) therapies against solid cancers

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-Ts should thereby be able to detect and efficiently kill cancer cells.

This approach to immunotherapy aims to overcome the patient's tolerance to cancer cells and tumor-induced immunosuppression by activating the patient's T cells outside the body, genetically modifying them with tumor-specific TCRs and finally multiplying them. In this way, large numbers of specific T cells are made available to patients to fight the cancer within a short period of time.

As Medigene's development of enhanced TCR-Ts progressed, both at the level of TCRs themselves as well as the enhancements such as the PD1-41BB switch receptor, the opportunity to gain a competitive advantage in the treatment of solid tumors became more apparent. In this context, the strategic decision was made to focus Medigene's resources on advancing its programs against solid tumors. The corollary of this strategic new focus on solid cancers is that the Company's developments against hematological indications would thereafter only be continued with partners contingent on the achievement of critical data points.

Based on patient numbers and the unmet medical need in the area of solid tumors, Medigene believes that this will be the most significant commercial opportunity for its clearly differentiated technologies.

### 2.1.1 MDG10XX – Enhancing the safety and activity of TCR-T therapies in the treatment of solid tumor indications

TCR-4 is Medigene's lead TCR candidate against solid tumors – a non-mutated TCR isolated using Medigene's high-throughput screening platform from a healthy donor that, in the context of human leukocyte antigen (HLA) A2, specifically recognizes a peptide stemming from the PRAME protein. PRAME is an antigen of the cancer-testis antigen family which is expressed by a variety of solid cancer types. TCR-4 is highly sensitive for this PRAME epitope and its activity has been demonstrated both *in vitro* (against a variety of tumor cell types including lung cancer, uterine carcinoma, melanoma, and ovarian cancer, among others) and in an *in vivo* model against melanoma.

The PD1-41BB switch receptor is the most advanced of the enhancements currently being developed by Medigene. Solid tumors grow in our bodies through the development of mechanisms to hide from the immune system and evade T cell attacks, such mechanisms including the expression of the checkpoint molecule PD-L1 on their surface. Medigene's PD1-41BB switch receptor turns the tumor's off-signal sent by PD-L1 into an activation signal for the TCR-T cells.

As shown at the American Association for Cancer Research (AACR) and the Association for Cancer Immunotherapy (CIMT) virtual meetings in March and May 2021, respectively, addition of the PD1-41BB switch receptor improved the effector function of TCR-T cells carrying the TCR-4 *in vitro* in an environment with repeated exposure to tumor cells mimicking the real-life situation in solid cancers.

Finally, with the presentation at the digital TCR-based Therapies Summit in June 2021, these observations were confirmed *in vivo*. The new data came from a very challenging *in vivo* model of aggressively growing, PD-L1 positive melanoma and showed that only TCR-T cells carrying the combination of both TCR-4 and PD1-41BB could eliminate tumors with these highly immunosuppressive characteristics.

Cytokine analysis of the dual-equipped TCR-T cells was presented at the European Society for Medical Oncology (ESMO) Congress in September 2021. Among them, a significantly higher proportion of polyfunctional T cells were found, which were able to release four to ten cytokines simultaneously- messenger molecules for immune cells. The expression of effector and stimulatory cytokines as well as chemo-attractive cytokines, which help the T cells to migrate to their target tissue in the body, was particularly enhanced.

### 2.1.2 Identification of TCRs against unique new tumor-specific antigens (TSAs)

In January 2020, Medigene entered into a research collaboration focusing on novel cancer antigens for highly specific immunotherapies with the University of Montréal. The identification of novel TSAs as targets for T cells represents a vital goal for the development of effective and safe cancer immunotherapies.

Under the collaboration agreement, Medigene gained access to 47 potential TSAs presented by one of five common HLA types that were identified as novel peptides eluted from the HLA molecules of tumor cells. 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, giving them the character of TSAs.

As presented at the AACR virtual meeting, Medigene's high-throughput screening technology identified ten peptides as immunogenic and able to induce specific T cell responses. One or more immunogenic peptides were found for each of the five analyzed HLA types. TCRs of T cell clones recognizing these novel peptides were determined by gene sequencing and their continuing further characterization was presented at the CIMT virtual meeting.

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. For example, at the Society for Immunotherapy of Cancer's (SITC) Annual Meeting currently taking place, Medigene is presenting data on the validation of TCR candidates from three healthy donors. Responses from Medigene's TCR-T cells expressing these TCRs to cultured ovarian tumor cells are orders of magnitude higher than those against cultured normal ovarian cells.

### 2.1.3 Extension of patent portfolio

Medigene constantly expands its patent portfolio around new technologies as well as existing patents into further jurisdictions.

In January 2021, Medigene reported that it was granted patents around its technologies in significant territories including both the USA and Europe. The US-patent US10,858,760 covers Medigene's TCR building block library that enables rapid reconstruction and testing of newly discovered human TCR sequences. The European patent EP3394247A1 will cover Medigene's CrossTAg-1 technology and the US-patent US10,882,891 covers the use of the CrossTAg technology in dendritic cells (DCs) and DC vaccines. This technology allows cross-presentation of antigens on both HLA class I and II molecules thereby stimulating both killer T cells and helper T cells, respectively. These major T cell subsets play key roles in immune responses, including those against cancer.

## 2.2 Immunotherapies against blood cancer

### 2.2.1 MDG1011

"MDG1011" is Medigene's first clinical TCR-T immunotherapy product candidate and targets the tumor antigen PRAME. Medigene is conducting a multi-center, open-label Phase I/II clinical trial of MDG1011 to treat blood cancer patients with advanced-stage acute myeloid leukemia (AML) or myelodysplastic syndrome (MDS).

The Phase I part is a dose escalation trial which primarily evaluates safety and feasibility as well as other secondary endpoints. Patient recruitment was almost not affected by the ongoing COVID-19 pandemic. In June 2021, the last patient was recruited into the third dose cohort of the Phase I part and topline data are expected to be published by the end of 2021.

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

### 2.2.2 MDG1021

Mid-2020, a Phase I trial of MDG1021, a TCR-T therapy directed against the HA-1 antigen, was initiated at the Leiden University Medical Center (LUMC), the Netherlands. Medigene in-licensed the HA-1-specific TCR from the LUMC at the end of 2018. The study was designed to recruit patients suffering from relapsed or persistent blood cancers after allogeneic (non-self) hematopoietic stem cell transplantation.

Consistent with the company's decision to focus its development efforts on solid cancers, the MDG1021 development program was discontinued in January 2021 and patient recruitment was put on hold. All rights to the HA-1-specific TCR, as well as sponsorship of the Phase I clinical trial, were transferred to Miltenyi Biotec B.V. & Co. KG (Miltenyi) in July 2021. From now on, Miltenyi will continue the development of this program.

### 2.2.3 Dendritic cell (DC) vaccines

Medigene has developed a new generation of antigen-tailored DC vaccines. The positive results of the completed open-label Phase I/II clinical 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 consistent clinical benefit without experiencing serious adverse events (SAEs) associated with treatment. However, as Medigene's development focus is on TCR-T therapies, the DC vaccine project will only be continued with partners.

Recently, a competing product was newly approved as maintenance therapy for patients with AML by the FDA in the U.S. and Medigene expects similar approvals to be granted soon in other regions including China. Medigene is monitoring the approval processes with regard to further developments. For the Asian region, a development partnership exists with Cytovant Sciences HK Limited, a biopharmaceutical company founded by Roivant Sciences (Roivant/Cytovant). Current events affect the development of the DC vaccine under this partnership as well as Medigene’s further partnering efforts regarding the DC vaccine project.

## 2.3 Development partnerships

Medigene plans to continue the successful collaborations with its existing partners and will continue to evaluate new partnering opportunities related to its portfolio of product candidates to maximize the Company’s value and secure funding for the further development of its product candidates.

### 2.3.1 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.

As reported previously, Medigene’s preclinical activities under the partnership were unaffected by the ongoing COVID-19 pandemic in 2021.

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 ImmunoTherpay of Cancer* (*JITC*) and received the "Best Immune Cell Therapies and Immune Cell Engineering Paper Award" from SITC.

### 2.3.2 TCR-T and DC partnership with Roivant/Cytovant

In 2019, Medigene entered into license and cooperation agreements with Roivant/Cytovant, which cover a TCR which is directed against the tumor antigen NY-ESO-1, two TCR-T development projects of which one started in April 2020 as well as Medigene’s DC vaccine, for Asia including the People’s Republic of China, Hong Kong, Macao, Taiwan, South Korea, and Japan.

The COVID-19 situation in the Asian region, according to Medigene's current knowledge, does not relevantly affect development activities of Roivant/Cytovant. Preclinical work by Medigene within the framework of this partnership is also progressing unaffected by the pandemic.

### 2.4 Changes in the Executive Management Board

At the end of March 2021, Dr. Kai Pinkernell, former Chief Medical Officer and Chief Development Officer (CMO&CDO), left the Company's Executive Management Board for personal reasons. Since then, Dr. René Goedkoop holds the role of acting CMO and is responsible for the continuation of Medigene's clinical projects, primarily the finalization of the Phase I part of the clinical trial with MDG1011 in patients with AML or MDS.

Dr. Goedkoop previously has held several CMO positions in international biopharmaceutical companies such as Sensimed S.A., Lausanne, Switzerland, EryDel S.p.A., Bresso (Milan), Italy, or Pharnext S.A., Paris, France, and has had a lead role already in Medigene's clinical trials as Vice President Clinical Affairs since January 2019. Dr. Pinkernell continued to support Medigene in an advisory role until the end of September 2021.

# 3 FINANCIAL DEVELOPMENT AND FORECAST

Total revenues increased by €622 k to €6,478 k as of 30 September 2021 (30 September 2020: €5,856 k). This is due to higher revenues resulting from research and development services from strategic partnerships. Total revenues also include revenues from the reversal of contractual liabilities. Research and development expenses of €8,806 k as of 30 September 2021 are €7,791 k lower than in the previous year (30 September 2020: €16,597 k), mainly due to the stronger focus on certain TCR-T therapies for the treatment of solid tumors (MDG10XX). As a result, earnings before interest, taxes, depreciation and amortization (EBITDA) are €10,318 k higher than in the previous year (30 September 2020: €-16,526 k) and amount to €-6,208 k as of 30 September 2021.

In the third quarter of 2021, Medigene sold all its remaining shares in Immunocore Holdings Ltd., consisting of 162,035 ordinary shares, net of transaction costs for approx. US-$4.7 m. However, research and development expenses to advance Medigene's clinical and preclinical activities are still the main reason for the decrease in cash and cash equivalents and time deposits as of 30 September 2021. As of 30 September 2021, cash and cash equivalents amounted to €23,200 k (31 December 2020: €30,033 k).

In October 2021, a milestone from the agreement with Roivant/Cytovant in the amount of US-$2 m was realized. The received milestone payment as well as reduced research and development expenses, which are now better estimated towards the year end, reflect cost-saving measures achieved as part of the strategic focus on solid tumors in 2020, and enabled Medigene to improve its financial guidance for the fiscal year 2021, as first published with the Annual Report 2020.

The forecast for total revenues has been increased from previously €7-9 m to a range of €10-11 m and the forecast for research and development costs has been reduced from previously €14-20 m to a range of €11-12 m. As a result, the forecast for the expected EBITDA loss has improved to €7-9 m (previously €10-17 m). Based on its current planning, the Company remains financed into the first quarter of 2023.

Currently, Medigene does not expect the COVID-19 pandemic to have a material impact on total revenues, research and development expenses and EBITDA loss in 2021.

# 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 2020, as these have remained largely unchanged since the approval of the 2020 Consolidated Financial Statements on 19 March 2021.

Medigene continues to regularly review its risk assessment regarding the COVID-19 pandemic and will make updates as appropriate (see above for program-specific COVID-19 comments).

The occurrence of any one of the risks described above or 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

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|---|---|
| Annual Report 2021 | 23 March 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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