

February 2, 2021



# Medexus Pharmaceuticals and medac GmbH enter into a License Agreement for First-in-Class Conditioning Agent for Hematopoietic Stem Cell Transplantation, Treosulfan, in the United States

*Orphan Designated Drug with August 2021 PDUFA date*

*Management to host conference call at 10:00 AM Eastern Time on February 3, 2021 and*

*Key Opinion Leader webinar to be held at 2:00 PM Eastern Time on February 5, 2021*

TORONTO and CHICAGO and MONTREAL and WEDEL, Germany, Feb. 02, 2021 (GLOBE NEWSWIRE) -- Medexus Pharmaceuticals Inc. ("**Medexus**") (TSXV: MDP) (OTCQX: MEDXF) (Frankfurt: P731) is pleased to announce that it and its wholly-owned United States-based subsidiary, Medexus Pharma, Inc. ("**Medexus Pharma**" and together with Medexus, the "**Company**") entered into a Commercialization and Supply Agreement with medac Gesellschaft für klinische Spezialpräparate m.b.H. ("**medac**"), pursuant to which medac has granted Medexus Pharma an exclusive license to commercialize treosulfan, a bifunctional alkylating agent, in the United States (the "**License Agreement**").

Treosulfan is an innovative, orphan-designated agent developed for use as part of a conditioning treatment for patients undergoing allogeneic hematopoietic stem cell transplantation ("**allo-HSCT**"). If approved by the U.S. Food and Drug Administration ("**FDA**"), the Company expects that a treosulfan-based regimen will be the first in a new conditioning treatment class, Reduced Toxicity Conditioning, resulting in a unique combination of improved survival outcomes compared to reduced-intensity regimens and decreased toxicity compared to standard myeloablative regimens. A Prescription Drug User Free Act ("**PDUFA**") date to review the New Drug Application ("**NDA**") in respect of treosulfan by the FDA has been scheduled for August 2021.

The Company intends to leverage its strong, existing commercial infrastructure in the United States to address the underserved allo-HSCT market through its commercialization of treosulfan. medac conducted a phase III randomized study (the "**Phase III Study**") comparing the results of treosulfan-based therapy with busulfan-based reduced intensity conditioning in advance of allo-HSCT for adult patients with acute myeloid leukemia ("**AML**") and myelodysplastic syndrome ("**MDS**") who were considered ineligible for standard myeloablative conditioning regimens. The planned confirmatory interim analysis of the Phase III Study demonstrated that non-inferiority was achieved in the treosulfan group compared to the busulfan group in two-year event-free survival with 64.0% (95% CI 56.0–70.9) in the treosulfan group and 50.4% (95% CI 42.8–57.5) in the busulfan group (HR 0.65

[95% CI 0.47–0.90]);  $p=0.0000164$  (adjusted  $p$ -value for testing non-inferiority of treosulfan compared to busulfan).<sup>1</sup> Despite lacking indications for use in patients with AML or MDS, busulfan is the current market leading alkylating agent for allo-HSCT. Prior to genericization in 2016, busulfan reached peak annual sales of U.S. \$126 million in the United States.<sup>2</sup>

The NDA in respect of treosulfan was filed by medac in August 2020 and seeks FDA approval for use of treosulfan as part of a conditioning regimen for allo-HSCT for adults with AML and MDS. The NDA is supported by the completed follow-up results from the Phase III Study covering all 570 randomized patients including superiority testing, which may result in even stronger claims than non-inferiority in a final label for treosulfan, if approved by the FDA.<sup>3</sup>

On April 8, 2015, the FDA granted medac Orphan Drug Designation for treosulfan as a conditioning treatment prior to allo-HSCT in malignant and non-malignant disease in adults and pediatric patients. In accordance with the Orphan Drug Act, seven years of exclusivity for this indication is expected upon FDA approval. According to the most recent data from the Center for International Blood & Marrow Transplant Research (CIBMTR), there were an estimated 9,028 allo-HSCT procedures in the United States in 2018, growing at about 3% year over year. Another 14,006 autologous-HSCT (auto-HSCT) procedures, which also routinely feature conditioning regimens that include alkylating agents, were completed that same year.<sup>4</sup>

Treosulfan was granted marketing authorization in combination with fludarabine by the European Commission in June 2019, indicated for use in combination with fludarabine as part of a conditioning treatment prior to allo-HSCT in (i) adult patients with both malignant and non-malignant diseases, and (ii) pediatric patients older than one month with malignant diseases. In Canada, Medexus is currently distributing treosulfan via the Special Access Program.

H. Joachim Deeg, MD, Professor of Medical Oncology at the University of Washington School of Medicine, Professor of Clinical Research at the Fred Hutchinson Cancer Research Center, and Physician at the Seattle Cancer Care Alliance, commented, “Treosulfan has proven to be a potent drug for transplant conditioning in several phase II trials for both malignant and non-malignant disorders, conducted at our own Center and several other institutions, earning the label ‘high intensity, low toxicity’. Of note, clinically meaningful improvements in favor of the treosulfan group for event-free survival, overall survival, and transplant-related mortality were seen in medac’s study, and a treosulfan-based regimen promises to be the preferred standard conditioning therapy for this study population, which represents the growing population of older and comorbid patients with AML or MDS, and beyond.”

Mary Horowitz, MD, MS, Professor of Hematologic Research at the Medical College of Wisconsin and Scientific Director for the CIBMTR, commented, “It is incredibly important for clinicians to have more options for patients undergoing allo-HSCT. I am very happy to see that medac and Medexus have teamed up to work towards bringing treosulfan to the U.S. market. The data on treosulfan thus far is highly encouraging, suggesting it could fill an important gap for higher risk patients who cannot tolerate the typical toxicity profile of currently available high-intensity conditioning regimens.”

## The License Agreement

Upon entering into the License Agreement, Medexus Pharma paid medac a non-refundable upfront payment of U.S. \$5 million. Under the terms of the License Agreement, Medexus Pharma must also pay medac (i) up to an aggregate of U.S. \$55 million in non-refundable regulatory milestone payments, contingent upon the achievement of certain regulatory events in connection with the FDA's review process (the "**Regulatory Milestone Payments**"), and (ii) up to an aggregate of U.S. \$40 million in non-refundable sales milestone payments, contingent upon Medexus Pharma's achievement of certain net sales goals (the "**Sales Milestone Payments**", and together with the Regulatory Milestone Payments, the "**Milestone Payments**"). In addition, Medexus Pharma will pay medac a low single-digit royalty on its net sales of treosulfan in the United States.

The License Agreement is effective as of today and continues until the 10<sup>th</sup> anniversary of FDA approval of the initial NDA, unless earlier terminated by either the Company or medac in accordance with their respective rights under the License Agreement. Going forward, medac will continue with primary responsibility for development and regulatory matters in respect of treosulfan, including preparing and obtaining FDA approval of the initial NDA. After such FDA approval, Medexus Pharma will maintain regulatory approval of treosulfan in the United States and leverage its significant commercial experience in leading the commercialization effort for treosulfan. medac will also be responsible for the manufacturing and supply of treosulfan to Medexus Pharma in accordance with the terms of the License Agreement. The Company and medac will work together to finalize the preparations for commercialization of treosulfan ahead of the PDUFA date and expect to launch shortly after FDA approval.

Ken d'Entremont, Chief Executive Officer of Medexus, stated, "We are pleased to execute another transformative transaction with medac. In 2018, when we acquired medac's U.S. affiliate, we anticipated that treosulfan could be a significant advancement in HSCT. This transaction marks another major milestone for Medexus and is indicative of our continued effort to further expand into the U.S. through what we believe will be a highly accretive transaction for the Company. Given the drug's therapeutic profile and the data generated to date, we believe that treosulfan could exceed peak sales of busulfan of U.S. \$126 million from use in allo-HSCT alone. This belief is re-enforced by the fact that busulfan is currently being used off-label for the indications for which treosulfan has Orphan Drug Designation. Importantly, we believe there is a large unmet need as the current standard of care is not suitable for numerous at-risk groups, due to the high toxicity effects. Treosulfan has demonstrated excellent event-free survival and overall survival among such groups and as a result, should be well positioned to become the new standard of care in the U.S., with more than 100 publications supporting the safety and efficacy of treosulfan. We are proud to be working towards providing patients with a new solution that could have a very meaningful impact on their lives."

Jörg Hans, Chief Executive Officer of medac, emphasizes, "This licensing deal with Medexus offers us the unique opportunity of providing patients and physicians with our very promising new treatment option in the area of allogeneic hematopoietic stem cell transplantation now also in the United States. The treosulfan-based conditioning regimen stands out for its combination of being highly effective - similar to the potency of the myeloablative procedure - while simultaneously exhibiting significantly reduced toxicity. We

at medac are very proud of our first-in-class conditioning agent as it addresses a huge need in the area of conditioning treatments especially with regard to high-risk patients. Therefore, this product fully meets our company goals of improving patients' quality of life and supporting healthcare professionals in the best possible way. As a shareholder in Medexus we see the expansion of our relationship as a true win-win."

Medexus and Medexus Pharma were represented by Munsch Hardt Kopf and Harr, P.C. and medac was represented by Baker & McKenzie LLP with respect to the License Agreement.

### **Conference Call Details**

Medexus will host a conference call on February 3, 2021 at 10:00 AM Eastern Time (U.S. and Canada) to discuss the License Agreement and to provide an operational update.

The conference call will be available via telephone by dialing toll free 888-506-0062 for Canadian and U.S. callers or 973-528-0011 for international callers, or on the Medexus' Investor Events section of the website: [https://www.medexus.com/en\\_US/investors/news-events](https://www.medexus.com/en_US/investors/news-events).

A webcast replay will be available on Medexus' Investor Events section of the website ([https://www.medexus.com/en\\_US/investors/news-events](https://www.medexus.com/en_US/investors/news-events)) through May 3, 2021. A telephone replay of the call will be available approximately one hour following the call, through February 10, 2021 and can be accessed by dialing 877-481-4010 for Canadian and U.S. callers or 919-882-2331 for international callers and entering conference ID: 39898

### **Key Opinion Leader Webinar**

Medexus will be hosting a Key Opinion Leader webinar to discuss treosulfan on February 5, 2021 at 2:00 PM Eastern Time (U.S. and Canada), followed by a question-and-answer period. Ken d'Entremont, CEO, will be joined by H. Joachim Deeg, MD to discuss the clinical data supporting treosulfan.

To join the webinar, please register here: [Treosulfan Key Opinion Leader Webinar](#). After registering, you will receive a confirmation email containing information about joining the webinar. The webinar will also be live streamed on YouTube for those who are unable to use Zoom: [YouTube Live Stream](#).

Questions may be asked during the webinar or can be emailed ahead of time to [info@adcap.ca](mailto:info@adcap.ca). A replay will be made available on the Medexus website.

### **H. Joachim Deeg, MD**

H. Joachim Deeg, MD, is a Physician at the Seattle Cancer Care Alliance, a Professor of Medical Oncology at the University of Washington School of Medicine, and a Professor of Clinical Research at the Fred Hutchinson Cancer Research Center. He currently holds the Miklos Kohary and Natalia Zimonyi Kohary Endowed Chair for Cancer Research. He is an expert in bone marrow transplantation, myelodysplastic syndromes, and myeloproliferative neoplasms. Dr. Deeg is a board-certified oncologist with more than 40 years of experience treating blood-disorders. He has a medical degree from the University of Bonn School of Medicine. Dr. Deeg completed his residency at the University of Rochester, NY and did a fellowship in Hematology/Oncology at the Fred Hutchinson Cancer Research Center/

University of Washington, Seattle.

### **Mary Horowitz, MD**

Dr. Horowitz is the Robert A. Uihlein Professor of Hematologic Research and Deputy Cancer Center at the Medical College of Wisconsin in Milwaukee. She is also Scientific Director Emeritus of the Center for International Blood and Marrow Transplant Research (CIBMTR). The CIBMTR is a research collaboration between the National Marrow Donor Program<sup>®</sup> (NMDP)/Be The Match<sup>®</sup> and the Medical College of Wisconsin. The CIBMTR collaborates with the global scientific community to advance hematopoietic cell transplantation and cellular therapy worldwide to increase survival and enrich quality of life for patients. The CIBMTR facilitates critical observational and interventional research through scientific and statistical expertise, a large network of transplant centers, and a unique and extensive clinical outcomes database. Dr. Horowitz also leads the Coordinating Center of the U.S. Blood and Marrow Clinical Trials Network, a multicenter group funded by the National Institutes of Health to test new therapies to improve the safety and effectiveness of transplantation. She has co-authored more than 400 publications addressing diverse issues in clinical BMT.

<sup>1</sup> *Beelen, DW et al., Final Results of a Prospective Randomized Multicenter Phase III Trial Comparing Treosulfan / Fludarabine to Reduced Intensity Conditioning with Busulfan / Fludarabine Prior to Allogeneic Hematopoietic Stem Cell Transplantation in Elderly or Comorbid Patients with Acute Myeloid Leukemia or Myelodysplastic Syndrome. Blood. 2017;130 (Suppl 1):521*

<sup>2</sup> *Symphony Health PHAST Data 2020*

<sup>3</sup> *Beelen, DW et al. Final Evaluation of a Clinical Phase III Trial Comparing Treosulfan to Busulfan-Based Conditioning Therapy Prior to Allogeneic Hematopoietic Stem Cell Transplantation of Adult Acute Myeloid Leukemia and Myelodysplastic Syndrome Patients Ineligible to Standard Myeloablative Regimens. Biol Blood Marrow Transplant 25 (2019) S1-S6, p. 53, Abstract No. 04.*

<sup>4</sup> *D'Souza, A, Fretham C, Lee SJ, et al. Current Use of and Trends in Hematopoietic Cell Transplantation in the United States. Biol Blood Marrow Transplant. 2020 May 11: S1083-8791(20)30225-1*

### **About medac GmbH**

medac GmbH is a privately held, global pharmaceutical company with a growing pharmaceutical and diagnostics business. Since its foundation in Germany in 1970, medac has been specializing in the treatment of diseases within the indication areas oncology, hematology, urology and autoimmune disorders. medac is committed to the refinement of existing and the development of new therapeutic products – always with the focus on improving patients' quality of life. medac has become known for developing innovative products also in less common indications. This dedication has resulted in a comprehensive portfolio of pharmaceutical products that help make a difference in the lives of patients. medac continually invests in its product development and manufacturing as well as logistic capacities to meet both patients' needs and the demands of healthcare professionals.

## **About Medexus Pharmaceuticals Inc.**

Medexus is a leading innovative and rare disease company with a strong North American commercial platform. From a foundation of proven best in class products we are building a highly differentiated company with a portfolio of innovative and high value orphan and rare disease products that will underpin our growth for the next decade. The Company's vision is to provide the best healthcare products to healthcare professionals and patients, through our core values of Quality, Innovation, Customer Service and Teamwork. Medexus Pharmaceuticals is focused on the therapeutic areas of auto-immune disease, hematology, and allergy. The Company's leading products are: Rasuvo™ and Metoject®, a unique formulation of methotrexate (auto-pen and pre-filled syringe) designed to treat rheumatoid arthritis and other auto-immune diseases; IXINITY®, an intravenous recombinant factor IX therapeutic for use in patients 12 years of age or older with Hemophilia B – a hereditary bleeding disorder characterized by a deficiency of clotting factor IX in the blood, which is necessary to control bleeding; and Rupall®, an innovative prescription allergy medication with a unique mode of action.

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### **Forward Looking Statements**

Certain statements made in this press release contain forward-looking information within the meaning of applicable securities laws ("**forward-looking statements**"). The words

“anticipates,” “believes,” “expects,” “should”, “will,” and similar expressions are often intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Specific forward-looking statements contained in this press release include, but are not limited to, statements with respect to the August 2021 PDUFA date, expectations for treosulfan to be the first in a new conditioning treatment class, the Company’s intention to leverage its commercial infrastructure in the United States to commercialize treosulfan, the expectation for exclusivity for treosulfan upon FDA approval, the results of the Phase III Study and the possibility of non-inferiority or stronger claims in the final label for treosulfan, the expected launch of treosulfan, the accretive nature of the transaction, the potential for treosulfan to exceed peak sales of busulfan and the anticipated growth in sales of, the market for and distribution of, treosulfan. These statements are based on factors or assumptions that were applied in drawing a conclusion or making a forecast or projection, including assumptions based on historical trends, current conditions and expected future developments. Since forward-looking statements relate to future events and conditions, by their very nature they require making assumptions and involve inherent risks and uncertainties. The Company cautions that although it is believed that the assumptions are reasonable in the circumstances, these risks and uncertainties give rise to the possibility that actual results may differ materially from the expectations set out in the forward-looking statements. Material risk factors include those set out in the Company’s materials filed with the Canadian securities regulatory authorities from time to time, including the Company’s most recent annual information form and management’s discussion and analysis; future capital requirements; intellectual property protection and infringement risks; competition (including potential for generic competition); reliance on key management personnel; the Company’s ability to implement its business plan; the Company’s ability to leverage its United States and Canadian infrastructure to promote additional growth, including with respect to the infrastructure of Medexus Pharma, and the potential benefits the Company expects to derive therefrom; regulatory approval by the FDA; litigation risk; and government regulation. Given these risks, undue reliance should not be placed on these forward-looking statements, which apply only as of the date hereof. Other than as specifically required by law, the Company undertakes no obligation to update any forward-looking statements to reflect new information, subsequent or otherwise.



Source: Medexus Pharmaceuticals Inc