



## Media Release

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# MorphoSys Completes Enrollment of Phase 3 MANIFEST-2 Study of Pelabresib in Myelofibrosis with Topline Results Expected by End of 2023

*Enrollment of Phase 3 frontMIND study of tafasitamab in first-line diffuse large B-cell lymphoma is also complete*

MorphoSys AG (FSE: MOR; NASDAQ: MOR) announced today that enrollment is complete for MANIFEST-2, the ongoing Phase 3 study exploring the efficacy and safety of pelabresib, an investigational BET inhibitor, in combination with ruxolitinib versus ruxolitinib alone in patients with myelofibrosis who have not previously been treated with a JAK inhibitor (JAK inhibitor-naïve). The topline data are now expected by the end of 2023, earlier than previously anticipated.

Myelofibrosis – which belongs to a group of diseases called myeloproliferative disorders – is a difficult-to-treat form of blood cancer with limited treatment options. JAK inhibitors are a current standard of care treatment for myelofibrosis, which focus on relieving symptoms of the disease rather than treating its cause. But, with this treatment strategy, only about half of patients attain adequate disease control, and durability of response is often limited. Clinical data suggest synergistic effects between BET inhibition and JAK inhibition in myelofibrosis, supporting the potential of this combination therapy.

“With so many patients left behind by current treatment options for myelofibrosis, there is a critical need for regimens that elevate the standard of care for patients suffering from this debilitating disease,” said Tim Demuth, M.D., Ph.D., Chief Research and Development Officer, MorphoSys. “Now that MANIFEST-2 has completed enrollment earlier than anticipated, we look forward to the coming insights into the therapeutic potential of pelabresib in combination with ruxolitinib for JAK inhibitor-naïve patients with myelofibrosis. MANIFEST-2 is the latest milestone in our efforts to improve outcomes for blood cancer patients and is a testament to our continued commitment to the myelofibrosis community.”

MANIFEST-2 is a global, multicenter, double-blind, Phase 3 study of more than 400 patients who were naïve to JAK inhibitors. Patients were randomized 1:1 to pelabresib in combination with ruxolitinib or placebo plus ruxolitinib. The primary endpoint of the trial is the proportion of patients who achieve a 35% or greater reduction in spleen volume at week 24 (known as SVR35). Reduction in spleen size is an important clinical endpoint in myelofibrosis because spleen enlargement reflects disease activity and can cause significant pain and discomfort.

The key secondary endpoint is the proportion of patients achieving a 50% or greater improvement in total symptom score, as measured by the Myelofibrosis Symptom Assessment Form v4.0, at week 24. Patients with myelofibrosis experience a severely diminished quality of life due to symptoms such as severe fatigue, fever and weight loss. The Myelofibrosis Symptom Assessment Form is a validated self-assessment tool designed specifically for myelofibrosis patients that can track changes in these symptoms.

The MANIFEST-2 trial is supported by findings from the Phase 2 MANIFEST trial of pelabresib in combination with ruxolitinib in patients with myelofibrosis, including those who were JAK inhibitor-naïve. Updated [results from MANIFEST](#) presented at the American Society of

Hematology 2022 Annual Meeting and Exposition suggest that pelabresib in combination with ruxolitinib provided prolonged improvement in both spleen size and symptom severity at and beyond 24 weeks.

Enrollment of the Phase 3 *frontMIND* study is also complete, with more than 880 patients enrolled in the trial. *frontMIND* is a global, multicenter, randomized, double-blind, placebo-controlled trial exploring tafasitamab, marketed in the U.S. as Monjuvi® and outside the U.S. by Incyte as Minjuvi®, plus lenalidomide in addition to R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone) versus R-CHOP alone as a first-line treatment for high-intermediate and high-risk patients with diffuse large B-cell lymphoma. The topline data from this study are expected in the second half of 2025.

#### **About Pelabresib**

Pelabresib (CPI-0610) is an investigational selective small molecule designed to promote anti-tumor activity by inhibiting the function of bromodomain and extra-terminal domain (BET) proteins to decrease the expression of abnormally expressed genes in cancer. Pelabresib is being investigated as a treatment for myelofibrosis and has not yet been evaluated or approved by any regulatory authorities.

#### **About Myelofibrosis**

Myelofibrosis – one of a group of diseases called myeloproliferative disorders – is a difficult-to-treat form of blood cancer that's characterized by bone marrow fibrosis (a buildup of scar tissue in the bone marrow), spleen enlargement and anemia (low red blood cell counts) often requiring periodic blood transfusions. Patients with myelofibrosis can also suffer from a range of physical symptoms, including severe fatigue, night sweats, itching, increased bleeding and significant pain caused by their enlarged spleen. For many living with myelofibrosis, the combination of symptoms often severely impacts their quality of life. At diagnosis, several factors, such as age, genetics and bloodwork, help determine a patient's long-term prognosis. About 90% of newly diagnosed patients have intermediate- to high-risk disease, which has a worse prognosis and a higher likelihood of disease-associated symptoms. Today, myelofibrosis treatments revolve around the use of medications called JAK inhibitors, which focus on relieving symptoms of myelofibrosis rather than treating its cause. But with this strategy, only about 50% of patients achieve adequate symptom control, and, unfortunately, that relief fades with time for many. Patients suffering from myelofibrosis are in critical need of treatment options that not only address their symptoms but also change the overall course of their disease.

#### **About MANIFEST-2**

[MANIFEST-2 \(NCT04603495\)](#) is a global, double-blind, randomized Phase 3 clinical trial with pelabresib in combination with ruxolitinib versus placebo plus ruxolitinib in JAK inhibitor-naïve patients with myelofibrosis. The primary endpoint of the study is a 35% or greater reduction in spleen volume (SVR35) from baseline at 24 weeks. The key secondary endpoint of the study is a 50% or greater improvement in total symptom score (TSS50) from baseline at 24 weeks. Constellation Pharmaceuticals, Inc., a MorphoSys company, is the MANIFEST-2 trial sponsor.

#### **About MANIFEST**

[MANIFEST \(NCT02158858\)](#) is an open-label Phase 2 clinical trial of pelabresib in patients with myelofibrosis. The MANIFEST trial is evaluating pelabresib in combination with ruxolitinib in JAK-inhibitor-naïve myelofibrosis patients (Arm 3), with a primary endpoint of the proportion of patients with a ≥35% spleen volume reduction from baseline (SVR35) after 24 weeks of treatment. The trial is also evaluating pelabresib either as a monotherapy in patients who are resistant to, intolerant of, or ineligible for ruxolitinib and no longer on the drug (Arm 1) or as add-on therapy in combination with ruxolitinib in patients with a suboptimal response to ruxolitinib or myelofibrosis progression (Arm 2). Patients in Arms 1 and 2 are being stratified based on transfusion-dependent (TD) status. The primary endpoint for the patients in cohorts 1A and 2A, who were TD at baseline, is conversion to transfusion independence for 12 consecutive weeks. The primary endpoint for patients in cohorts 1B and 2B, who were not TD at baseline, is the proportion of patients with a ≥35% spleen volume reduction from baseline after 24 weeks of treatment. Constellation Pharmaceuticals, Inc., a MorphoSys company, is the MANIFEST trial sponsor.

#### **About Monjuvi® (tafasitamab-cxix)**

Tafasitamab is a humanized Fc-modified CD19 targeting immunotherapy. In 2010, MorphoSys licensed exclusive worldwide rights to develop and commercialize tafasitamab from Xencor, Inc. Tafasitamab incorporates an XmAb® engineered Fc domain, which mediates B-cell lysis through apoptosis and immune effector mechanism including Antibody-Dependent Cell-Mediated Cytotoxicity (ADCC) and Antibody-Dependent Cellular Phagocytosis (ADCP).

In the United States, Monjuvi® (tafasitamab-cxix) is approved by the U.S. Food and Drug Administration in combination with lenalidomide for the treatment of adult patients with relapsed or refractory DLBCL not otherwise specified, including DLBCL arising from low grade lymphoma, and who are not eligible for autologous stem cell transplant (ASCT). This indication is approved under accelerated approval based on overall response rate. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).

In Europe, Minjuvi® (tafasitamab) received conditional marketing authorization in combination with lenalidomide, followed by Minjuvi monotherapy, for the treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) who are not eligible for autologous stem cell transplant (ASCT).

Tafasitamab is being clinically investigated as a therapeutic option in B-cell malignancies in several ongoing combination trials.

Monjuvi® and Minjuvi® are registered trademarks of MorphoSys AG. Tafasitamab is co-marketed by Incyte and MorphoSys under the brand name Monjuvi® in the U.S., and marketed by Incyte under the brand name Minjuvi® in Europe and Canada.

XmAb® is a registered trademark of Xencor, Inc.

## **Important Safety Information**

### **What are the possible side effects of MONJUVI?**

MONJUVI may cause serious side effects, including:

- Infusion reactions. Your healthcare provider will monitor you for infusion reactions during your infusion of MONJUVI. Tell your healthcare provider right away if you get fever, chills, rash, flushing, headache, or shortness of breath during an infusion of MONJUVI.
  
- Low blood cell counts (platelets, red blood cells, and white blood cells). Low blood cell counts are common with MONJUVI, but can also be serious or severe. Your healthcare provider will monitor your blood counts during treatment with MONJUVI. Tell your healthcare provider right away if you get a fever of 100.4 F (38 C) or above, or any bruising or bleeding.
  
- Infections. Serious infections, including infections that can cause death, have happened in people during treatments with MONJUVI and after the last dose. Tell your healthcare provider right away if you get a fever of 100.4 F (38 C) or above, or develop any signs and symptoms of an infection.

The most common side effects of MONJUVI include:

- Feeling tired or weak
- Diarrhea
- Cough
- Fever
- Swelling of lower legs or hands
- Respiratory tract infection
- Decreased appetite

These are not all the possible side effects of MONJUVI.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

**Before you receive MONJUVI, tell your healthcare provider about all your medical conditions, including if you:**

- Have an active infection or have had one recently.
  
- Are pregnant or plan to become pregnant. MONJUVI may harm your unborn baby. You should not become pregnant during treatment with MONJUVI. Do not receive treatment with MONJUVI in combination with lenalidomide if you are pregnant because lenalidomide can cause birth defects and death of your unborn baby.
  - You should use an effective method of birth control (contraception) during treatment and for at least 3 months after your final dose of MONJUVI.

-Tell your healthcare provider right away if you become pregnant or think that you may be pregnant during treatment with MONJUVI.

-Are breastfeeding or plan to breastfeed. It is not known if MONJUVI passes into your breastmilk. Do not breastfeed during treatment for at least 3 months after your last dose of MONJUVI.

**You should also read the lenalidomide Medication Guide for important information about pregnancy, contraception, and blood and sperm donation.**

**Tell your healthcare provider about all the medications you take**, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

**Call your doctor for medical advice about side effects. You may report side effects to the FDA at (800) FDA-1088 or [www.fda.gov/medwatch](http://www.fda.gov/medwatch). You may also report side effects to MORPHOSYS US INC. at (844) 667-1992.**

Please see the full [Prescribing Information](#) for MONJUVI, including Patient Information, for additional Important Safety Information.

#### **About Diffuse Large B-cell Lymphoma (DLBCL)**

DLBCL is the most common type of non-Hodgkin lymphoma in adults worldwide, characterized by rapidly growing masses of malignant B-cells in the lymph nodes, spleen, liver, bone marrow or other organs. It is an aggressive disease with about 40% of patients not responding to initial therapy or relapsing thereafter, leading to a high medical need for new, effective therapies, especially for patients who are not eligible for an autologous stem cell transplant in this setting.

#### **About frontMIND**

The [frontMIND \(NCT04824092\)](#) trial is a randomized, double-blind, placebo-controlled, global Phase 3 clinical study in previously untreated high-intermediate and high-risk DLBCL patients that is conducted in partnership with the German Lymphoma Association (GLA), the Italian Lymphoma study group and the US Oncology Network. The study enrolled more than 880 DLBCL patients to receive either tafasitamab plus lenalidomide in addition to rituximab, cyclophosphamide, doxorubicin, vincristine and prednisone (R-CHOP) or R-CHOP alone. The primary endpoint is investigator-assessed progression-free survival, according to Lugano 2014 criteria, and key secondary endpoints include event-free survival by investigator, overall survival, metabolic complete response rate by a Blinded Independent Review Committee, and overall response rate.

#### **About MorphoSys**

At MorphoSys, we are driven by our mission: *More life for people with cancer*. As a global commercial-stage biopharmaceutical company, we develop and deliver innovative medicines to patients, aspiring to redefine how cancer is treated. MorphoSys is headquartered in Planegg, Germany, and has its U.S. operations anchored in Boston, Massachusetts. To learn more, visit us at [www.morphosys.com](http://www.morphosys.com) and follow us on [Twitter](#) and [LinkedIn](#).

#### **Forward Looking Statements**

*This communication contains certain forward-looking statements concerning the MorphoSys group of companies. The forward-looking statements contained herein represent the judgment of MorphoSys as of the date of this release and involve known and unknown risks and uncertainties, which might cause the actual results, financial condition and liquidity, performance or achievements of MorphoSys, or industry results, to be materially different from any historic or future results, financial conditions and liquidity, performance or achievements expressed or implied by such forward-looking statements. In addition, even if MorphoSys' results, performance, financial condition and liquidity, and the development of the industry in which it operates are consistent with such forward-looking statements, they may not be predictive of results or developments in future periods. Among the factors that may result in differences are that MorphoSys' expectations may be incorrect, the inherent uncertainties associated with competitive developments, clinical trial and product development activities and regulatory approval requirements, MorphoSys' reliance on collaborations with third parties, estimating the commercial potential of its development programs and other risks indicated in the risk factors included in MorphoSys' Annual Report on Form 20-F and other filings with the U.S. Securities and Exchange Commission. Given these uncertainties, the reader is advised not to place any undue reliance on such forward-looking statements. These forward-looking statements speak only as of the date of publication of this document. MorphoSys expressly disclaims any obligation to update any such forward-looking statements in this document to reflect any change in its expectations with regard thereto or any change in events, conditions or circumstances on which any such statement is based or that may affect the likelihood that actual results will differ from those set forth in the forward-looking statements, unless specifically required by law or regulation.*

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