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For Immediate Release

DARZALEX *FASPRO*® (daratumumab and hyaluronidase-fihj)-based quadruplet therapy regimen shows significant improvement in outcomes for patients with transplant-eligible newly diagnosed multiple myeloma

DARZALEX FASPRO®-based induction, consolidation and maintenance regimen reduced risk of progression or death by 58 percent compared to standard of care regimen

First presentation of data from Phase 3 PERSEUS study highlighted in late-breaking abstract session at ASH 2023 and simultaneously published in The New England Journal of Medicine

SAN DIEGO (December 12, 2023) – Johnson & Johnson announced today the first data from the Phase 3 PERSEUS study highlighting significant clinical improvement with a DARZALEX *FASPRO*® (daratumumab and hyaluronidase-fihj)-based quadruplet induction, consolidation regimen and doublet maintenance regimen in the treatment of transplant-eligible (TE) newly diagnosed multiple myeloma (NDMM). The data, showing an unrivaled progression-free survival (PFS) in a Phase 3 study evaluating TE NDMM and clinically significant improvement of rates of overall complete response (CR) or better and minimal residual disease (MRD) negativity over the comparator arm, were featured as a late-breaking oral presentation at the 2023 American Society of Hematology (ASH) Annual Meeting (Abstract #LBA-1). The data were published simultaneously in *The New England Journal of Medicine*.

The PERSEUS study, conducted in collaboration with the European Myeloma Network, found that induction and consolidation treatment with DARZALEX *FASPRO*® in combination with bortezomib, lenalidomide and dexamethasone (D-VRd), followed by DARZALEX *FASPRO*® and lenalidomide (D-R) maintenance, reduced the risk of disease progression or death by 58 percent (Hazard Ratio [HR], 0.42; 95 percent Confidence Interval [CI] 0.30-0.59; *P* <0.0001), compared to bortezomib, lenalidomide and dexamethasone (VRd) alone followed by lenalidomide (R) maintenance.[1] The quadruplet regimen also significantly increased the depth of response compared to treatment with VRd alone, with higher rates of CR or better, stringent complete response (sCR), and MRD negativity.

“The progression-free survival that was achieved in transplant-eligible patients who were treated with the daratumumab-based induction, consolidation and maintenance therapy regimen is unprecedented in a Phase 3 clinical study evaluating this patient population, but is not unexpected as these findings build on a number of studies that previously demonstrated clinical benefit with daratumumab-based regimens in this patient population,” said Pieter Sonneveld, M.D., Ph.D., Professor of Hematology at the Erasmus University of Rotterdam and Chair of the Erasmus MC Cancer Institute, Rotterdam, Netherlands.‡ “The results we see across clinically relevant subgroups, including in patients who present with advanced disease or who are considered high risk, are promising for clinicians who are on the frontlines of treating patients who are newly diagnosed with this complex disease.”

The estimated 48-month PFS rates were 84.3 percent for D-VRd vs 67.7 percent for VRd. The consistent PFS improvement with D-VRd vs VRd was observed across most clinically relevant subgroups, including patients with International Staging System (ISS) stage III disease (HR, 0.42; 95 percent CI, 0.22-0.83) or high cytogenetic risk (HR, 0.59; 95 percent CI, 0.36-0.99). Treatment with D-VRd also resulted in deeper responses compared with VRd, including higher rates of sCR (69.3 percent vs 44.6 percent; *P* <0.0001), and ≥CR (87.9 percent vs 70.1 percent; *P* <0.0001). Overall MRD negativity rates (10^{-5}) were higher with D-VRd vs VRd (75.2 percent vs 47.5 percent; *P* <0.0001). Sustained MRD-negativity rates (for ≥12 months) more than doubled with D-VRd (64.8 percent vs 29.7 percent; *P* <0.0001). Overall survival (OS) data are not yet mature but trending favorably for the D-VRd arm compared to VRd.

“We now have evidence supporting this DARZALEX-based quadruplet induction and consolidation regimen and doublet maintenance regimen as a potential new standard of care in transplant-eligible disease, complementing data from the Phase 3 MAIA study, which firmly established a DARZALEX-based triplet therapy as standard of care in transplant-ineligible disease,” said Craig Tendler, M.D., Vice President, Late Development and Global Medical Affairs, Johnson & Johnson Innovative Medicine. “We will continue to advance innovative regimens and approaches with DARZALEX to deliver on our commitment of transforming outcomes for patients with multiple myeloma.”

The overall safety profile of D-VRd was consistent with the known safety profiles for daratumumab and VRd. The most common (>10 percent) Grade 3/4 hematologic and non-hematologic adverse events (AE) with D-VRd vs VRd were neutropenia (62.1 percent vs 51.0 percent), thrombocytopenia (29.1 percent vs 17.3 percent), diarrhea (10.5 percent vs 7.8 percent), pneumonia (10.5 percent vs 6.1 percent) and febrile neutropenia (9.4 percent vs 10.1 percent).

About the PERSEUS study

The PERSEUS study is being conducted in collaboration with the European Myeloma Network as sponsor. PERSEUS is an ongoing, randomized, open-label, Phase 3 study comparing the efficacy and safety of D-VRd followed by D-R maintenance vs VRd followed by R maintenance in patients with transplant-eligible NDMM. The primary endpoint was PFS, and secondary endpoints included overall CR or better rate, overall MRD-negativity (in patients with CR or better), and overall survival. The median age is 61.0 (32-70) years for patients in the D-VRd arm and 59.0 (31-70) years for patients in the VRd arm. The study is being conducted in 14 countries in Europe and Australia.

About multiple myeloma

Multiple myeloma is an incurable blood cancer that affects a type of white blood cell called plasma cells, which are found in the bone marrow.[2] In multiple myeloma, these plasma cells change, spread rapidly and replace normal cells in the bone marrow with tumors.[3] Multiple myeloma is the third most common blood cancer and remains an incurable disease.[4] In 2023, it is estimated that more than 35,000 people will be diagnosed with multiple myeloma in the U.S. and more than 12,000 people will die from the disease.[5] People living with multiple myeloma have a 5-year survival rate of 59.8 percent.[6] While some people diagnosed with multiple myeloma initially have no symptoms, most patients are diagnosed due to symptoms that can include bone fracture or pain, low red blood cell counts, tiredness, high calcium levels and kidney problems or infections.[7,8]

About DARZALEX *FASPRO*® and DARZALEX®

DARZALEX *FASPRO*® (daratumumab and hyaluronidase-fihj) received U.S. FDA approval in May 2020 and is approved for eight indications in multiple myeloma, three of which are for frontline treatment in newly diagnosed patients who are transplant eligible or ineligible.[9] It is the only subcutaneous CD38-directed antibody approved to treat patients with MM. DARZALEX *FASPRO*® is co-formulated with recombinant human hyaluronidase PH20 (rHuPH20), Halozyme's ENHANZE® drug delivery technology.

DARZALEX® (daratumumab) received U.S. FDA approval in November 2015 and is approved in eight indications, three of which are in the frontline setting, including newly diagnosed patients who are transplant eligible and ineligible.[10]

DARZALEX® is the first CD38-directed antibody approved to treat multiple myeloma.[11] DARZALEX®-based regimens have been used in the treatment of more than 422,000 patients worldwide and more than 68,000 patients in the U.S. alone.

In August 2012, Janssen Biotech, Inc. and Genmab A/S entered a worldwide agreement, which granted Janssen an exclusive license to develop, manufacture and commercialize daratumumab.

Since 2020, the National Comprehensive Cancer Network® (NCCN®) has recommended daratumumab-based combination regimens for the treatment of newly diagnosed multiple myeloma and relapsed and refractory multiple myeloma.† For newly diagnosed multiple myeloma in non-transplant candidates, the NCCN® guidelines recommend daratumumab in combination with lenalidomide and dexamethasone as a Category 1 preferred regimen; daratumumab in combination with bortezomib, melphalan, and prednisone as another recommended Category 1 regimen; and daratumumab in combination with bortezomib, cyclophosphamide, and prednisone as another recommended Category 2A regimen. For newly diagnosed multiple myeloma in transplant candidates, the NCCN® guidelines recommend daratumumab in combination with bortezomib, lenalidomide and dexamethasone as another recommended Category 2A regimen; daratumumab in combination with bortezomib, thalidomide and dexamethasone as a Category 2A regimen useful in certain circumstances; daratumumab in combination with carfilzomib, lenalidomide and dexamethasone as a Category 2A regimen useful in certain circumstances; and daratumumab in combination with cyclophosphamide, bortezomib and dexamethasone as a Category 2A regimen useful in certain circumstances. For maintenance in transplant candidates, the NCCN guidelines recommend daratumumab in combination with lenalidomide as useful in certain circumstances. In relapsed/refractory myeloma, four daratumumab regimens are listed as Category 1 preferred regimens for early relapses (1-3 prior therapies): daratumumab in combination with lenalidomide and dexamethasone; daratumumab in combination with bortezomib and dexamethasone; daratumumab in combination with carfilzomib and dexamethasone; and daratumumab in combination with pomalidomide and dexamethasone [after one prior therapy including lenalidomide and a proteasome inhibitor (PI)]. The NCCN® also recommends daratumumab in combination with cyclophosphamide, bortezomib and dexamethasone as another Category 2A regimen for early relapses (1-3 prior therapies) and as monotherapy as a Category 2A regimen useful in certain circumstances for early relapse patients after at least three prior therapies, including a PI and an immunomodulatory agent, or for patients who are double refractory to a PI and an immunomodulatory agent.

For more information, visit www.DARZALEX.com.

DARZALEX *FASPRO*® IMPORTANT SAFETY INFORMATION

INDICATIONS

DARZALEX *FASPRO*® (daratumumab and hyaluronidase-fihj) is indicated for the treatment of adult patients with multiple myeloma:

- In combination with bortezomib, melphalan, and prednisone in newly diagnosed patients who are ineligible for autologous stem cell transplant
- In combination with lenalidomide and dexamethasone in newly diagnosed patients who are ineligible for autologous stem cell transplant and in patients with relapsed or refractory multiple myeloma who have received at least one prior therapy
- In combination with bortezomib, thalidomide, and dexamethasone in newly diagnosed patients who are eligible for autologous stem cell transplant
- In combination with pomalidomide and dexamethasone in patients who have received at least one prior line of therapy including lenalidomide and a proteasome inhibitor
- In combination with carfilzomib and dexamethasone in patients with relapsed or refractory multiple myeloma who have received one to three prior lines of therapy
- In combination with bortezomib and dexamethasone in patients who have received at least one prior therapy
- As monotherapy in patients who have received at least three prior lines of therapy including a proteasome inhibitor (PI) and an immunomodulatory agent or who are double-refractory to a PI and an immunomodulatory agent

CONTRAINDICATIONS

DARZALEX *FASPRO*® is contraindicated in patients with a history of severe hypersensitivity to daratumumab, hyaluronidase, or any of the components of the formulation.

WARNINGS AND PRECAUTIONS

Hypersensitivity and Other Administration Reactions

Both systemic administration-related reactions, including severe or life-threatening reactions, and local injection-site reactions can occur with DARZALEX *FASPRO*®. Fatal reactions have been reported with daratumumab-containing products, including DARZALEX *FASPRO*®.

Systemic Reactions

In a pooled safety population of 898 patients with multiple myeloma (N=705) or light chain (AL) amyloidosis (N=193) who received DARZALEX *FASPRO*® as monotherapy or in combination, 9% of patients experienced a systemic administration-related reaction (Grade 2: 3.2%, Grade 3: 1%). Systemic administration-related reactions occurred in 8% of patients with the first injection, 0.3% with the second injection, and cumulatively 1% with subsequent injections. The median time to onset was 3.2 hours (range: 4 minutes to 3.5 days). Of the 140 systemic administration-related reactions that occurred in 77 patients, 121 (86%) occurred on the day of DARZALEX *FASPRO*® administration. Delayed systemic administration-related reactions have occurred in 1% of the patients.

Severe reactions included hypoxia, dyspnea, hypertension, tachycardia, and ocular adverse reactions, including choroidal effusion, acute myopia, and acute angle closure glaucoma. Other signs and symptoms of systemic administration-related reactions may include respiratory symptoms, such as bronchospasm, nasal congestion, cough, throat irritation, allergic rhinitis, and wheezing, as well as anaphylactic reaction, pyrexia, chest pain, pruritus, chills, vomiting, nausea, hypotension, and blurred vision.

Pre-medicate patients with histamine-1 receptor antagonist, acetaminophen, and corticosteroids. Monitor patients for systemic administration-related reactions, especially following the first and second injections. For anaphylactic reaction or life-threatening (Grade 4) administration-related reactions, immediately and permanently discontinue DARZALEX *FASPRO*®. Consider administering corticosteroids and other medications after the administration of DARZALEX *FASPRO*® depending on dosing regimen and medical history to minimize the risk of delayed (defined as occurring the day after administration) systemic administration-related reactions.

Ocular adverse reactions, including acute myopia and narrowing of the anterior chamber angle due to ciliochoroidal effusions with potential for increased intraocular pressure or glaucoma, have occurred with daratumumab-containing products. If ocular symptoms occur, interrupt DARZALEX *FASPRO*® and seek immediate ophthalmologic evaluation prior to restarting DARZALEX *FASPRO*®.

Local Reactions

In this pooled safety population, injection-site reactions occurred in 8% of patients, including Grade 2 reactions in 0.7%. The most frequent (>1%) injection-site reaction was injection-site erythema. These local reactions occurred a median of 5 minutes (range: 0 minutes to 6.5 days) after starting administration of DARZALEX *FASPRO*®. Monitor for local reactions and consider symptomatic management.

Neutropenia

Daratumumab may increase neutropenia induced by background therapy. Monitor complete blood cell counts periodically during treatment according to manufacturer's prescribing information for background therapies. Monitor patients with neutropenia for signs of infection. Consider withholding DARZALEX *FASPRO*® until recovery of neutrophils. In lower body weight patients receiving DARZALEX *FASPRO*®, higher rates of Grade 3-4 neutropenia were observed.

Thrombocytopenia

Daratumumab may increase thrombocytopenia induced by background therapy. Monitor complete blood cell counts periodically during treatment according to manufacturer's prescribing information for background therapies. Consider withholding DARZALEX *FASPRO*® until recovery of platelets.

Embryo-Fetal Toxicity

Based on the mechanism of action, DARZALEX *FASPRO*® can cause fetal harm when administered to a pregnant woman. DARZALEX *FASPRO*® may cause depletion of fetal immune cells and decreased bone density. Advise pregnant women of the potential risk to a fetus. Advise females with reproductive potential to use effective contraception during treatment with DARZALEX *FASPRO*® and for 3 months after the last dose.

The combination of DARZALEX *FASPRO*® with lenalidomide, thalidomide, or pomalidomide is contraindicated in pregnant women because lenalidomide, thalidomide, and pomalidomide may cause birth defects and death of the unborn child. Refer to the lenalidomide, thalidomide, or pomalidomide prescribing information on use during pregnancy.

Interference with Serological Testing

Daratumumab binds to CD38 on red blood cells (RBCs) and results in a positive indirect antiglobulin test (indirect Coombs test). Daratumumab-mediated positive indirect antiglobulin test may persist for up to 6 months after the last daratumumab administration. Daratumumab bound to RBCs masks detection of antibodies to minor antigens in the patient's serum. The determination of a patient's ABO and Rh blood type are not impacted.

Notify blood transfusion centers of this interference with serological testing and inform blood banks that a patient has received DARZALEX *FASPRO*®. Type and screen patients prior to starting DARZALEX *FASPRO*®.

Interference With Determination of Complete Response

Daratumumab is a human immunoglobulin G (IgG) kappa monoclonal antibody that can be detected on both the serum protein electrophoresis (SPE) and immunofixation (IFE) assays used for the clinical monitoring of endogenous M-protein. This interference can impact the determination of complete response and of disease progression in some DARZALEX *FASPRO*®-treated patients with IgG kappa myeloma protein.

ADVERSE REACTIONS

In multiple myeloma, the most common adverse reaction (≥20%) with DARZALEX *FASPRO*® monotherapy is upper respiratory tract infection. The most common adverse reactions with combination therapy (≥20% for any combination) include fatigue, nausea, diarrhea, dyspnea, insomnia, headache, pyrexia, cough, muscle spasms, back pain, vomiting, hypertension, upper respiratory tract infection, peripheral sensory neuropathy, constipation, pneumonia, and peripheral edema.

The most common hematology laboratory abnormalities (≥40%) with DARZALEX *FASPRO*® are decreased leukocytes, decreased lymphocytes, decreased neutrophils, decreased platelets, and decreased hemoglobin.

Please click here to see the full Prescribing Information.

About Johnson & Johnson

At Johnson & Johnson, we believe health is everything. Our strength in healthcare innovation empowers us to build a world where complex diseases are prevented, treated, and cured, where treatments are smarter and less invasive, and solutions are personal. Through our expertise in Innovative Medicine and MedTech, we are uniquely positioned to innovate across the full spectrum of healthcare solutions today to deliver the breakthroughs of tomorrow, and profoundly impact health for humanity. Learn more at https://www.jnj.com/ or at www.janssen.com/johnson-johnson-innovative-medicine. Follow us at @JanssenUS and @JNJInnovMed. Janssen Research & Development, LLC and Janssen Biotech, Inc. are both Johnson & Johnson companies.

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Cautions Concerning Forward-Looking Statements

This press release contains "forward-looking statements" as defined in the Private Securities Litigation Reform Act of 1995 regarding product development of DARZALEX FASPRO®. The reader is cautioned not to rely on these forward-looking statements. These statements are based on current expectations of future events. If underlying assumptions prove inaccurate or known or unknown risks or uncertainties materialize, actual results could vary materially from the expectations and projections of Janssen Research & Development, LLC, Janssen Biotech, Inc., and/or Johnson & Johnson. Risks and uncertainties include, but are not limited to: challenges and uncertainties inherent in product research and development, including the uncertainty of clinical success and of obtaining regulatory approvals; uncertainty of commercial success; competition, including technological advances, new products and patents attained by competitors; challenges to patents; changes in behavior and spending patterns of purchasers of health care products and services; changes to applicable laws and regulations, including global health care reforms; and trends toward health care cost containment. A further list and descriptions of these risks, uncertainties and other factors can be found in Johnson & Johnson's Annual Report on Form 10-K for the fiscal year ended January 1, 2023, including in the sections captioned "Cautionary Note Regarding Forward-Looking Statements" and "Item 1A. Risk Factors," and in Johnson & Johnson's subsequent Quarterly Reports on Form 10-Q and other filings with the Securities and Exchange Commission. Copies of these filings are available online at www.sec.gov, www.jnj.com or on request from Johnson & Johnson. None of Janssen Research & Development, Janssen Biotech, Inc., nor Johnson & Johnson undertakes to update any forward-looking statement as a result of new information or future events or developments.

‡ *Prof. Sonneveld has provided consulting, advisory, and speaking services to Johnson and Johnson; he has not been paid for any media work.*

†*See the NCCN Guidelines for detailed recommendations, including other treatment options.*

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[1] Sonneveld P et al. Phase 3 randomized study of daratumumab (DARA) + bortezomib, lenalidomide, and dexamethasone (D-VRd) versus VRd alone in patients (Pts) with newly diagnosed multiple myeloma (NDMM) who are eligible for autologous stem cell transplantation (ASCT): primary results of the PERSEUS trial. 2023 ASH Annual Meeting – American Society of Hematology. December 2023.
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