



News Release

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Janssen to Highlight Science, Innovation and Advances in Robust Oncology Portfolio and Pipeline Through More Than 60 Data Presentations at ASCO and EHA

Studies spanning industry-leading hematologic malignancies portfolio and pipeline with new research in solid tumor therapies to highlight precision medicine and targeted therapy strategies

RARITAN, N.J., May 31, 2022 — The Janssen Pharmaceutical Companies of Johnson & Johnson announced today that new research and data from its robust oncology portfolio and pipeline of investigational therapies will be presented at the 2022 American Society of Clinical Oncology (ASCO) Annual Meeting, taking place June 3-7 in Chicago, and the European Hematology Association (EHA) 2022 Congress taking place in Vienna, Austria, June 9-12. More than 60 presentations from company-sponsored studies across the two congresses, including 14 oral presentations, will feature new data and updates for both approved and investigational therapies that are being studied for the treatment of multiple blood cancers and solid tumors.

“The science and data that we will present at ASCO and EHA highlight the breadth and depth of our oncology portfolio and pipeline, and our team’s commitment to advance and deliver innovative treatments for patients,” said Peter Lebowitz, M.D., Ph.D., Global Therapeutic Area Head, Oncology, Janssen Research & Development, LLC. “Our research and collaborations underscore a focused scientific strategy to deeply understand disease biology in working towards our ultimate goal of preventing, intercepting and one day curing cancer.”

Consistent with ASCO’s theme of Advancing Equitable Cancer Care Through Innovation, Janssen recognizes the importance of eliminating health inequities – from research and clinical trials to access and quality of care – to address the diverse needs of patients and ensure access to cancer therapies.

“We are committed to improving representation of real-world patient populations in our clinical development programs and providing access to clinical trials, especially for those in underserved communities,” said Craig Tendler, M.D., Vice President, Late Development and Global Medical Affairs, Janssen Research & Development, LLC. “We also look to support investigators, communities and sites to overcome obstacles in oncology clinical trial participation among racial and ethnic minorities so that everyone can benefit from the advances in oncology drug development, which may have a profound impact on the lives of all patients in the future.”

With nearly six million patients diagnosed annually across hematologic malignancies and prostate, lung and bladder cancers, there remains significant unmet need in the treatment of these complex cancers.¹ The latest research and data at ASCO and EHA will demonstrate Janssen’s commitment to exploring new vital science for patients in these areas through precision medicine, targeted therapies and novel platforms.

“At Janssen, part of our mission to reimagine cancer care includes working to drive better outcomes for patients,” said Tyrone Brewer, U.S. President, Oncology, Janssen Biotech, Inc. “The research presented at ASCO underscores our commitment to advancing science, treatment options and patient care across hematologic malignancies, lung cancer, prostate cancer and bladder cancer, and our continued focus on helping patients navigate their treatment journeys.”

Key ASCO and EHA data presentations include:

Leukemia & lymphoma

Janssen continues to study **IMBRUVICA**[®] (ibrutinib) with the goal of addressing unmet clinical needs and helping to improve outcomes for patients living with mantle cell lymphoma (MCL) and chronic lymphocytic leukemia (CLL). Data from the Phase 3 SHINE study evaluating IMBRUVICA[®] in combination with bendamustine and rituximab (BR) in older patients with previously untreated MCL will be featured as an oral presentation ([ASCO Oral Abstract: #7502](#)). Additionally, three-year follow-up data from the Phase 2 CAPTIVATE Fixed Duration cohort evaluating IMBRUVICA[®] plus venetoclax fixed duration treatment for previously untreated patients with CLL or small lymphocytic lymphoma (SLL) will be highlighted in a poster presentation ([ASCO Poster Abstract: #7519](#)). At EHA, additional data from the CAPTIVATE study will focus on synergistic activity and immune restoration with this combination regimen.

In acute lymphoblastic leukemia or lymphoblastic lymphoma, data from the Phase 2 DELPHINUS study will be featured in an oral presentation, reporting safety and efficacy results for the investigational use of **DARZALEX**[®] (daratumumab) in the treatment of pediatric and young adult patients with relapsed or refractory disease ([ASCO Oral Abstract: #10001](#); [EHA Poster Session: #P360](#)).

Multiple myeloma

With a portfolio of four therapies with distinct target antigens and different mechanisms of action, Janssen continues to focus on developing and delivering tailored immunotherapy regimens to treat patients with multiple myeloma. Data at ASCO and EHA will span frontline and relapsed or refractory settings with the latest updates from two investigational therapies and two approved treatments.

Two presentations will highlight treatment with DARZALEX[®] in combination with lenalidomide and dexamethasone in newly diagnosed multiple myeloma, including updated results from the Phase 3 MAIA study in transplant-ineligible patients ([ASCO Poster Abstract: #8044](#); [EHA Poster Session: #P936](#)), and the Phase 2 GRIFFIN study evaluating the investigational use of DARZALEX[®] in combination with bortezomib,

lenalidomide and dexamethasone in transplant-eligible patients ([ASCO Poster Abstract: #8011](#); [EHA Poster Session: #P934](#)). In relapsed or refractory disease, results from the POLLUX and CASTOR studies will report on treatment with DARZALEX® in combination with lenalidomide and dexamethasone and in combination with bortezomib and dexamethasone in patients who experienced early or late relapse following at least one prior therapy ([ASCO Poster Abstract: #8052](#); [EHA Poster Session: #P933](#)).

The latest data to be presented at ASCO and EHA for **CARVYKTI™** (ciltacabtagene autoleucel; cilta-cel), Janssen's first approved cell therapy, will include longer-term efficacy and safety results from the CARTITUDE-1 study and cohorts A and B of the CARTITUDE-2 study. Both studies include patients with relapsed or refractory multiple myeloma (ASCO Poster Abstracts: [#8020](#), [#8029](#), [#8028](#); [EHA Oral Abstract: #S185](#)).

Data at ASCO and EHA for the investigational bispecific antibody **teclistamab** (BCMAxCD3 bispecific antibody) will include an updated analysis from the Phase 1/2 MajesTEC-1 study evaluating monotherapy treatment for patients with relapsed or refractory multiple myeloma ([ASCO Oral Abstract: #8007](#); [EHA Poster Abstract: #P921](#)) and results from an analysis of patients who were previously treated with a BCMA-targeted agent ([ASCO Poster Abstract: #8013](#); [EHA Oral Abstract: #S184](#)). Additionally, updated results from the TRIMM-2 study of teclistamab in combination with **DARZALEX FASPRO®** (daratumumab and hyaluronidase-fihj) in patients with relapsed or refractory multiple myeloma will be presented in an oral session at ASCO and EHA ([ASCO Poster Abstract: #8032](#); [EHA Oral Abstract: #S188](#)).

Updated results from the Phase 1 MonumentAL-1 study of the investigational bispecific antibody **talquetamab** (GPRC5DxCD3 bispecific antibody) as a monotherapy treatment for highly refractory multiple myeloma will be reported ([ASCO Poster Abstract: #8015](#); [EHA Oral Abstract: #S182](#)). In addition, updated Phase 1b results from the TRIMM-2 study evaluating talquetamab in combination with DARZALEX FASPRO® for the treatment of relapsed or refractory patients with multiple myeloma will be highlighted ([EHA Oral Abstract: #S183](#)).

Biomarker-driven solid tumors

Janssen's first presentation of tumor-agnostic data will share interim analysis results from the Phase 2 RAGNAR study evaluating the investigational use of **BALVERSA**[®] (erdafitinib) in patients with advanced or metastatic solid tumors with fibroblast growth factor receptor (FGFR) alterations ([ASCO Oral Abstract: #3007](#)). The interim analysis comprises a patient population with 32 distinct solid tumor histologies.

Lung cancer

Updated data will be presented for the bispecific antibody **RYBREVANT**[®] (amivantamab-vmjw) that highlights Janssen's commitment to precision medicine strategies, with an oral presentation of updated results for RYBREVANT[®] as a monotherapy in patients with non-small cell lung cancer (NSCLC) characterized by MET exon 14 skipping mutations ([ASCO Oral Abstract: #9008](#)).

A second oral presentation of the CHRYSALIS-2 study of the investigational combination of RYBREVANT[®] and lazertinib in patients with exon 19 deletion or L858R EGFR-mutated NSCLC ([ASCO Oral Abstract: #9006](#)) will also be reported.

Prostate cancer

A gene-by-gene analysis will provide new insights from the prospectively designed Phase 3 MAGNITUDE study, which is evaluating the safety and efficacy of the combination of **niraparib** and abiraterone acetate plus prednisone in patients with homologous recombination repair (HRR)-gene mutated metastatic castration-resistant prostate cancer (mCRPC). The data evaluated HRR gene alterations beyond BRCA1/2, including PALB 2, CHEK2 and other mutations ([ASCO Poster Abstract: #5020](#)).

Janssen will present baseline patient characteristics and the application of different radiation therapy regimens from the Phase 3 ATLAS study investigating if the addition of **ERLEADA**[®] (apalutamide) to a gonadotropin-releasing hormone agonist (GnRH) in participants with high-risk, localized or locally advanced prostate cancer receiving primary radiation therapy results in an improvement of metastasis-free survival ([ASCO Poster Abstract: #5084](#)).

A complete list of Janssen-sponsored abstracts at ASCO and EHA is available at: [Janssen.com/ASCO2022](https://www.janssen.com/ASCO2022).

About IMBRUVICA®

IMBRUVICA® (ibrutinib) is a once-daily oral medication that is jointly developed and commercialized by Janssen Biotech, Inc. and Pharmacyclics LLC, an AbbVie company. IMBRUVICA® blocks the Bruton's tyrosine kinase (BTK) protein, which is needed by normal and abnormal B cells, including specific cancer cells, to multiply and spread. By blocking BTK, IMBRUVICA® may help move abnormal B cells out of their nourishing environments and inhibits their proliferation.^{2,3,4}

IMBRUVICA® is approved in more than 100 countries for at least one indication and has been used to treat more than 250,000 patients worldwide. There are more than 50 company-sponsored clinical trials, including 18 Phase 3 studies, over 11 years evaluating the efficacy and safety of IMBRUVICA®.

IMBRUVICA® was first approved by the U.S. Food and Drug Administration (FDA) in November 2013, and today is indicated for adult patients in six disease areas, including five hematologic cancers. These include indications to treat adults with CLL/SLL with or without 17p deletion (del17p), and adults with Waldenström's macroglobulinemia (WM), and adult patients with previously treated mantle cell lymphoma (MCL)*, as well as to treat adult patients with previously treated marginal zone lymphoma (MZL) who require systemic therapy and have received at least one prior anti-CD20-based therapy*, and adult patients with previously treated chronic graft-versus-host disease (cGVHD) after failure of one or more lines of systemic therapy.⁵

**Accelerated approval was granted for MCL and MZL based on overall response rate. Continued approval for MCL and MZL may be contingent upon verification and description of clinical benefit in confirmatory trials.*

The National Comprehensive Cancer Network® (NCCN®), recommends ibrutinib (IMBRUVICA®) as a preferred regimen for the initial treatment of CLL/SLL and has Category 1 treatment status for treatment-naïve patients without deletion 17p/TP53 mutation and as a preferred treatment for treatment-naïve patients with deletion 17p/TP53 mutation. The NCCN Guidelines also recommend IMBRUVICA®, with or without rituximab, as a preferred regimen for the treatment of relapsed/refractory MCL,

as a Category 1 preferred regimen for both untreated and previously treated WM patients, and as a preferred regimen for relapsed/refractory MZL.⁶

For more information, visit www.IMBRUVICA.com.

About DARZALEX FASPRO® and DARZALEX®

DARZALEX FASPRO® [received](#) U.S. FDA approval in May 2020 and is approved for eight indications in multiple myeloma (MM), three of which are for frontline treatment in newly diagnosed patients who are transplant eligible or ineligible.⁷ DARZALEX FASPRO® is the only subcutaneous CD38-directed antibody globally approved to treat patients with MM. DARZALEX FASPRO® is co-formulated with recombinant human hyaluronidase PH20 (rHuPH20), Halozyme's ENHANZE® drug delivery technology. In January 2021, DARZALEX FASPRO® became the first FDA-approved therapy for light chain amyloidosis. In [August 2012](#), Janssen Biotech, Inc. entered into an exclusive global license and development agreement with Genmab A/S to develop, manufacture, and commercialize DARZALEX®.⁸ DARZALEX® has been approved in eight indications, three of which are in the frontline setting, including for newly diagnosed patients who are transplant eligible as well as those who are ineligible.⁹

For more information, visit www.DARZALEX.com.

About CARVYKTI™

CARVYKTI™ (cilta-cel) [received](#) approval by the U.S. FDA in February 2022 for the treatment of adults with relapsed or refractory multiple myeloma after four or more prior lines of therapy, including a proteasome inhibitor, an immunomodulatory agent, and an anti-CD38 monoclonal antibody.¹⁰ CARVYKTI™ is a BCMA-directed, genetically modified autologous T-cell immunotherapy, which involves reprogramming a patient's own T cells with a transgene encoding a chimeric antigen receptor (CAR) that directs the CAR positive T cells to eliminate cells that express BCMA. BCMA is primarily expressed on the surface of malignant multiple myeloma B-lineage cells, as well as late-stage B cells and plasma cells. The CARVYKTI™ CAR protein features two BCMA-targeting single domain designed to confer high avidity against human BCMA. Upon binding to BCMA-expressing cells, the CAR promotes T-cell activation, expansion, and elimination of target cells.

In December 2017, Janssen Biotech, Inc. entered into an exclusive worldwide license and collaboration agreement with Legend Biotech USA, Inc. to develop and commercialize CARVYKTI™.

Cilta-cel received a PRIority MEdicines (PRIME) designation from the European Commission in April 2019, and the Orphan Drug Designation for cilta-cel from the European Commission in February 2020. In May 2022, Janssen [announced](#) that the European Commission (EC) granted conditional marketing authorisation of CARVYKTI™ (ciltacabtagene autoleucel; cilta-cel) for the treatment of adults with relapsed and refractory multiple myeloma (RRMM) who have received at least three prior therapies, including an immunomodulatory agent (IMiD), a proteasome inhibitor (PI) and an anti-CD38 antibody, and have demonstrated disease progression on the last therapy. In March 2022, Janssen announced that the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) has recommended marketing authorization of cilta-cel for the treatment of adults with relapsed and refractory multiple myeloma, who have received at least three prior therapies, including an IMiD, a PI and an anti-CD38 antibody and have demonstrated disease progression on the last therapy.

There are several ongoing Phase 3 clinical trials investigating CARVYKTI™ in earlier treatment settings, including first-line.

For more information, visit www.CARVYKTI.com.

About Teclistamab

Teclistamab is an off-the-shelf, T-cell redirecting, bispecific antibody targeting both BCMA (B-cell maturation antigen) and CD3, the T-cell receptor. BCMA is expressed at high levels on multiple myeloma cells.^{11,12,13,14,15} Teclistamab redirects CD3-positive T-cells to BCMA-expressing myeloma cells to induce killing of tumor cells.¹⁴

Teclistamab is currently being evaluated in several monotherapy and combination studies. In 2020, the European Commission and the U.S. FDA each granted teclistamab Orphan Drug Designation for the treatment of multiple myeloma. In January 2021 and May 2021, teclistamab [received](#) a PRIority MEdicines (PRIME) designation by the European Medicines Agency (EMA) and Breakthrough Therapy Designation (BTD) by the U.S. FDA, respectively. PRIME offers enhanced interaction and early dialogue to optimize drug

development plans and speed up evaluation of cutting-edge, scientific advances that target a high unmet medical need.¹⁶ The U.S. FDA granted teclistamab Priority Review Designation in December 2021.

About Talquetamab

Talquetamab is a first-in-class, off-the-shelf, investigational T-cell redirecting bispecific antibody targeting both GPRC5D and CD3, a primary component of the T-cell receptor. GPRC5D is a novel target which is highly expressed on multiple myeloma cells.

Talquetamab is currently being evaluated in a Phase 1/2 clinical study for the treatment of relapsed or refractory multiple myeloma ([NCT03399799](#)) and is also being explored in combination studies ([NCT04586426](#)). In January 2021, talquetamab was granted PRIME designation by the European Commission. In 2021, the European Commission and the U.S. FDA each granted talquetamab Orphan Drug Designation for the treatment of multiple myeloma.

About BALVERSA®

BALVERSA® (erdafitinib) is a once-daily, oral FGFR kinase inhibitor that is [approved](#) by the U.S. FDA for the treatment of adults with locally advanced or metastatic urothelial carcinoma (mUC) that has susceptible FGFR3 or FGFR2 genetic alterations and has progressed during or following at least one line of platinum-containing chemotherapy, including within 12 months of neoadjuvant or adjuvant platinum-containing chemotherapy. Patients are selected for therapy based on an FDA-approved companion diagnostic for BALVERSA®. Information on FDA-approved tests for the detection of FGFR genetic alterations in urothelial cancer is available at:

<http://www.fda.gov/CompanionDiagnostics>. This indication is approved under accelerated approval based on tumor response rate. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.^{7,15}

In addition to RAGNAR, BALVERSA® is being studied in multiple clinical trials including the Phase 3 THOR ([NCT03390504](#)) study evaluating BALVERSA® versus standard of care, consisting of chemotherapy (docetaxel or vinflunine) or anti-PD-1 agent pembrolizumab, in participants with advanced urothelial cancer and selected FGFR aberrations with

disease progression following one prior line of therapy; and the Phase 2 THOR-2/BLC2003 study ([NCT04172675](https://clinicaltrials.gov/ct2/show/study/NCT04172675)) study examining BALVERSA® versus investigator choice of intravesical chemotherapy in participants who received Bacillus Calmette-Guérin and recurred with high risk non-muscle-invasive bladder cancer.^{16,17,18}

In 2008, Janssen entered into an exclusive worldwide license and collaboration agreement with Astex Pharmaceuticals to develop and commercialize BALVERSA®.

For more information, visit <https://www.BALVERSA.com>.

About RYBREVANT®

RYBREVANT® (amivantamab-vmjw) [received](#) accelerated approval by the U.S. FDA in May 2021 for the treatment of adult patients with locally advanced or metastatic NSCLC with EGFR exon 20 insertion mutations, as detected by an FDA-approved test, whose disease has progressed on or after platinum-based chemotherapy.¹⁷

This indication is approved under accelerated approval based on overall response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in the confirmatory trials.

The NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Non-Small Cell Lung Cancer* prefer NGS-based strategies over PCR-based approaches for the detection of EGFR exon 20 insertion variants and include amivantamab-vmjw (RYBREVANT®) as a subsequent therapy option with a Category 2A recommendation for patients that have progressed on or after platinum-based chemotherapy with or without immunotherapy and have EGFR exon 20 insertion mutation-positive advanced NSCLC.^{18††} RYBREVANT® has also received approval from health authorities in [Europe](#), as well as other markets around the world.

RYBREVANT® is being studied in multiple clinical trials, including the Phase 1/1b CHRYSALIS-2 ([NCT04077463](https://clinicaltrials.gov/ct2/show/study/NCT04077463)) study assessing the combination of RYBREVANT® and lazertinib in patients who have progressed after treatment with osimertinib and chemotherapy; as first-line therapy in untreated advanced EGFR-mutated NSCLC in the Phase 3 MARIPOSA ([NCT04487080](https://clinicaltrials.gov/ct2/show/study/NCT04487080)) study assessing amivantamab in combination with lazertinib; the planned Phase 3 MARIPOSA-2 ([NCT04988295](https://clinicaltrials.gov/ct2/show/study/NCT04988295)) study assessing the efficacy

of lazertinib, RYBREVANT® and carboplatin-pemetrexed versus carboplatin-pemetrexed in patients with locally advanced or metastatic EGFR exon 19 deletion or exon 21 L858R substitution NSCLC after osimertinib failure; the Phase 3 PAPHON (NCT04538664) study assessing RYBREVANT® in combination with carboplatin-pemetrexed versus chemotherapy alone in patients with advanced or metastatic EGFR-mutated NSCLC and exon 20 insertion mutations; and the Phase 1 PALOMA (NCT04606381) study assessing the feasibility of subcutaneous (SC) administration of RYBREVANT® based on safety and pharmacokinetics and to determine a dose, dose regimen and formulation for RYBREVANT® SC delivery.^{19,20,21,22,23,24}

* NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.

†See the NCCN Guidelines for detailed recommendations, including other treatment options.¹⁸

‡The NCCN Guidelines for NSCLC provide recommendations for certain individual biomarkers that should be tested and recommend testing techniques but do not endorse any specific commercially available biomarker assays or commercial laboratories.

For more information, visit: <https://www.RYBREVANT.com>.

About Lazertinib

Lazertinib is an oral, third-generation, brain-penetrant, EGFR tyrosine kinase inhibitor (TKI) that targets both the T790M mutation and activating EGFR mutations while sparing wild type-EGFR.²⁵ Interim safety and efficacy results from the lazertinib Phase 1-2 study were published in *The Lancet Oncology* in 2019. In 2018, Janssen Biotech, Inc. entered into a license and collaboration agreement with Yuhan Corporation for the development of lazertinib.

About Niraparib

Niraparib is an orally administered, poly-ADP ribose polymerase (PARP) inhibitor that is currently being studied by Janssen for the treatment of patients with prostate cancer. Ongoing studies include the Phase 3 [AMPLITUDE](#) study evaluating niraparib in

combination with abiraterone acetate plus prednisone in a biomarker-selected patient population with mCSPC; the Phase 3 [MAGNITUDE](#) study evaluating niraparib in combination with abiraterone acetate plus prednisone as a first-line treatment option compared to abiraterone acetate and prednisone plus placebo in adults with mCRPC; and [QUEST](#), a Phase 1b/2 study of niraparib combination therapies for the treatment of mCRPC. In April 2022, Janssen announced the submission of a Marketing Authorisation Application (MAA) to the European Medicines Agency (EMA) seeking approval of niraparib in combination with abiraterone acetate, in the form of a dual action tablet plus prednisone, based on the results of the Phase 3 MAGNITUDE study for the treatment of patients with prostate cancer who have progressed to metastatic castration-resistant prostate cancer (mCRPC) and are positive for homologous recombination repair (HRR) gene alterations.

In April 2016, Janssen Biotech, Inc. entered a worldwide (except Japan) collaboration and license agreement with TESARO, Inc. (acquired by GSK in 2018), for exclusive rights to niraparib in prostate cancer. In the U.S., niraparib is indicated for the maintenance treatment of adult patients with advanced epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in a complete or partial response to first-line platinum-based chemotherapy; for the maintenance treatment of adult patients with recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in a complete or partial response to platinum-based chemotherapy; for the treatment of adult patients with advanced ovarian, fallopian tube, or primary peritoneal cancer who have been treated with three or more prior chemotherapy regimens and whose cancer is associated with homologous recombination deficiency (HRD) positive status defined by either: a deleterious or suspected deleterious BRCA mutation, or genomic instability and who have progressed more than six months after response to the last platinum-based chemotherapy. In the EU, niraparib is indicated as monotherapy for the maintenance treatment of adult patients with advanced epithelial (FIGO Stages III and IV) high-grade ovarian, fallopian tube or primary peritoneal cancer who are in complete or partial response following platinum-based chemotherapy. Niraparib is currently marketed by GSK as ZEJULA[®].²⁶

About ERLEADA[®]

ERLEADA[®] (apalutamide) is an androgen receptor inhibitor indicated for the treatment of patients with non-metastatic castration-resistant prostate cancer (nmCRPC) and for the

treatment of patients with mCSPC.²⁷ ERLEADA[®] [received](#) U.S. FDA approval for nmCRPC in February 2018, and was [approved](#) for mCSPC in September 2019.²⁰ To date, more than 50,000 patients worldwide have been treated with ERLEADA[®].

For more information, visit www.ERLEADA.com.

IMBRUVICA[®] IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

Hemorrhage: Fatal bleeding events have occurred in patients who received IMBRUVICA[®]. Major hemorrhage (\geq Grade 3, serious, or any central nervous system events; e.g., intracranial hemorrhage [including subdural hematoma], gastrointestinal bleeding, hematuria, and post procedural hemorrhage) occurred in 4.2% of patients, with fatalities occurring in 0.4% of 2,838 patients who received IMBRUVICA[®] in 27 clinical trials. Bleeding events of any grade including bruising and petechiae occurred in 39%, and excluding bruising and petechiae occurred in 23% of patients who received IMBRUVICA[®], respectively.

The mechanism for the bleeding events is not well understood.

Use of either anticoagulant or antiplatelet agents concomitantly with IMBRUVICA[®] increases the risk of major hemorrhage. Across clinical trials, 3.1% of 2,838 patients who received IMBRUVICA[®] without antiplatelet or anticoagulant therapy experienced major hemorrhage. The addition of antiplatelet therapy with or without anticoagulant therapy increased this percentage to 4.4%, and the addition of anticoagulant therapy with or without antiplatelet therapy increased this percentage to 6.1%. Consider the risks and benefits of anticoagulant or antiplatelet therapy when co-administered with IMBRUVICA[®]. Monitor for signs and symptoms of bleeding.

Consider the benefit-risk of withholding IMBRUVICA[®] for at least 3 to 7 days pre- and post-surgery depending upon the type of surgery and the risk of bleeding.

Infections: Fatal and non-fatal infections (including bacterial, viral, or fungal) have occurred with IMBRUVICA[®] therapy. Grade 3 or greater infections occurred in 21% of

1,476 patients who received IMBRUVICA® in clinical trials. Cases of progressive multifocal leukoencephalopathy (PML) and *Pneumocystis jirovecii* pneumonia (PJP) have occurred in patients treated with IMBRUVICA®. Consider prophylaxis according to standard of care in patients who are at increased risk for opportunistic infections. Monitor and evaluate patients for fever and infections and treat appropriately.

Cardiac Arrhythmias, Cardiac Failure and Sudden Death: Fatal and serious cardiac arrhythmias and cardiac failure have occurred with IMBRUVICA®. Deaths due to cardiac causes or sudden deaths occurred in 1% of 4,896 patients who received IMBRUVICA® in clinical trials, including in patients who received IMBRUVICA® in unapproved monotherapy or combination regimens. These adverse reactions occurred in patients with and without preexisting hypertension or cardiac comorbidities. Patients with cardiac comorbidities may be at greater risk of these events.

Grade 3 or greater ventricular tachyarrhythmias were reported in 0.2%, Grade 3 or greater atrial fibrillation and atrial flutter were reported in 3.7%, and Grade 3 or greater cardiac failure was reported in 1.3% of 4,896 patients who received IMBRUVICA® in clinical trials, including in patients who received IMBRUVICA® in unapproved monotherapy or combination regimens. These events have occurred particularly in patients with cardiac risk factors including hypertension and diabetes mellitus, a previous history of cardiac arrhythmias, and in patients with acute infections.

Evaluate cardiac history and function at baseline, and monitor patients for cardiac arrhythmias and cardiac function. Obtain further evaluation (e.g., ECG, echocardiogram) as indicated for patients who develop symptoms of arrhythmia (e.g., palpitations, lightheadedness, syncope, chest pain), new onset dyspnea, or other cardiovascular concerns. Manage cardiac arrhythmias and cardiac failure appropriately, follow dose modification guidelines, and consider the risks and benefits of continued IMBRUVICA® treatment.

Hypertension: Hypertension occurred in 19% of 1,476 patients who received IMBRUVICA® in clinical trials. Grade 3 or greater hypertension occurred in 8% of patients. Based on data from 1,124 of these patients, the median time to onset was 5.9 months (range, 0.03 to 24 months). Monitor blood pressure in patients treated with IMBRUVICA®, initiate or adjust anti-hypertensive medication throughout treatment with

IMBRUVICA® as appropriate, and follow dosage modification guidelines for Grade 3 or higher hypertension.

Cytopenias: In 645 patients with B-cell malignancies who received IMBRUVICA® as a single agent, grade 3 or 4 neutropenia occurred in 23% of patients, grade 3 or 4 thrombocytopenia in 8% and grade 3 or 4 anemia in 2.8%, based on laboratory measurements. Monitor complete blood counts monthly.

Second Primary Malignancies: Other malignancies (10%), including non-skin carcinomas (3.9%), occurred among the 1,476 patients who received IMBRUVICA® in clinical trials. The most frequent second primary malignancy was non-melanoma skin cancer (6%).

Tumor Lysis Syndrome: Tumor lysis syndrome has been infrequently reported with IMBRUVICA®. Assess the baseline risk (e.g., high tumor burden) and take appropriate precautions. Monitor patients closely and treat as appropriate.

Embryo-Fetal Toxicity: Based on findings in animals, IMBRUVICA® can cause fetal harm when administered to a pregnant woman. Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment with IMBRUVICA® and for 1 month after the last dose. Advise males with female partners of reproductive potential to use effective contraception during the same time period.

ADVERSE REACTIONS

B-cell malignancies: The most common adverse reactions ($\geq 30\%$) in patients with B-cell malignancies (MCL, CLL/SLL, WM and MZL) were thrombocytopenia (54.5%)*, diarrhea (43.8%), fatigue (39.1%), musculoskeletal pain (38.8%), neutropenia (38.6%)*, rash (35.8%), anemia (35.0%)*, and bruising (32.0%).

The most common Grade ≥ 3 adverse reactions ($\geq 5\%$) in patients with B-cell malignancies (MCL, CLL/SLL, WM and MZL) were neutropenia (20.7%)*, thrombocytopenia (13.6%)*, pneumonia (8.2%), and hypertension (8.0%).

Approximately 9% (CLL/SLL), 14% (MCL), 14% (WM) and 10% (MZL) of patients had a dose reduction due to adverse reactions. Approximately 4-10% (CLL/SLL), 9% (MCL), and 7% (WM [5%] and MZL [13%]) of patients discontinued due to adverse reactions.

cGVHD: The most common adverse reactions ($\geq 20\%$) in patients with cGVHD were fatigue (57%), bruising (40%), diarrhea (36%), thrombocytopenia (33%)*, muscle spasms (29%), stomatitis (29%), nausea (26%), hemorrhage (26%), anemia (24%)*, and pneumonia (21%).

The most common Grade 3 or higher adverse reactions ($\geq 5\%$) reported in patients with cGVHD were pneumonia (14%), fatigue (12%), diarrhea (10%), neutropenia (10%)*, sepsis (10%), hypokalemia (7%), headache (5%), musculoskeletal pain (5%), and pyrexia (5%).

Twenty-four percent of patients receiving IMBRUVICA[®] in the cGVHD trial discontinued treatment due to adverse reactions. Adverse reactions leading to dose reduction occurred in 26% of patients.

*Treatment-emergent decreases (all grades) were based on laboratory measurements.

DRUG INTERACTIONS

CYP3A Inhibitors: Co-administration of IMBRUVICA[®] with strong or moderate CYP3A inhibitors may increase ibrutinib plasma concentrations. Increased ibrutinib concentrations may increase the risk of drug-related toxicity. Dose modifications of IMBRUVICA[®] are recommended when used concomitantly with posaconazole, voriconazole, and moderate CYP3A inhibitors. Avoid concomitant use of other strong CYP3A inhibitors. Interrupt IMBRUVICA[®] if strong inhibitors are used short-term (e.g., for ≤ 7 days). Avoid grapefruit and Seville oranges during IMBRUVICA[®] treatment, as these contain strong or moderate inhibitors of CYP3A. See dose modification guidelines in USPI sections 2.3 and 7.1.

CYP3A Inducers: Avoid coadministration with strong CYP3A inducers.

SPECIFIC POPULATIONS

Hepatic Impairment (based on Child-Pugh criteria): Avoid use of IMBRUVICA® in patients with severe hepatic impairment. In patients with mild or moderate impairment, reduce recommended IMBRUVICA® dose and monitor more frequently for adverse reactions of IMBRUVICA®.

Please [click here](#) to see the full Prescribing Information.

DARZALEX® (daratumumab) and DARZALEX FASPRO® (daratumumab and hyaluronidase-fihj) INDICATIONS AND IMPORTANT SAFETY INFORMATION

INDICATIONS

DARZALEX® (daratumumab) is indicated for the treatment of adult patients with multiple myeloma:

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

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 (PI)
- 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 PI and an immunomodulatory agent or who are double-refractory to a PI and an immunomodulatory agent

DARZALEX® AND DARZALEX FASPRO®: CONTRAINDICATIONS

DARZALEX® and DARZALEX FASPRO® are contraindicated in patients with a history of severe hypersensitivity to daratumumab, hyaluronidase (for DARZALEX FASPRO®), or any of the components of the formulations.

DARZALEX®: Infusion-Related Reactions

DARZALEX® can cause severe and/or serious infusion-related reactions including anaphylactic reactions. These reactions can be life-threatening, and fatal outcomes have been reported. In clinical trials (monotherapy and combination: N=2066), infusion-related reactions occurred in 37% of patients with the Week 1 (16 mg/kg) infusion, 2% with the Week 2 infusion, and cumulatively 6% with subsequent infusions. Less than 1% of patients had a Grade 3/4 infusion-related reaction at Week 2 or subsequent infusions. The median time to onset was 1.5 hours (range: 0 to 73 hours). Nearly all reactions occurred during infusion or within 4 hours of completing DARZALEX®. Severe reactions have occurred, including bronchospasm, hypoxia, dyspnea, hypertension, tachycardia, headache, laryngeal edema, pulmonary edema, and ocular adverse reactions, including choroidal effusion, acute myopia, and acute angle closure glaucoma.

Signs and symptoms may include respiratory symptoms, such as nasal congestion, cough, throat irritation, as well as chills, vomiting, and nausea. Less common signs and symptoms were wheezing, allergic rhinitis, pyrexia, chest discomfort, pruritus, hypotension, and blurred vision.

When DARZALEX® dosing was interrupted in the setting of ASCT (CASSIOPEIA) for a median of 3.75 months (range: 2.4 to 6.9 months), upon re-initiation of DARZALEX®, the incidence of infusion-related reactions was 11% for the first infusion following ASCT. Infusion-related reactions occurring at re-initiation of DARZALEX® following ASCT were consistent in terms of symptoms and severity (Grade 3 or 4: <1%) with those reported in previous studies at Week 2 or subsequent infusions. In EQUULEUS, patients receiving combination treatment (n=97) were administered the first 16 mg/kg dose at Week 1 split over two days, i.e., 8 mg/kg on Day 1 and Day 2, respectively. The incidence of any grade infusion-related reactions was 42%, with 36% of patients experiencing infusion-related reactions on Day 1 of Week 1, 4% on Day 2 of Week 1, and 8% with subsequent infusions.

Pre-medicate patients with antihistamines, antipyretics, and corticosteroids. Frequently monitor patients during the entire infusion. Interrupt DARZALEX[®] infusion for reactions of any severity and institute medical management as needed. Permanently discontinue DARZALEX[®] therapy if an anaphylactic reaction or life-threatening (Grade 4) reaction occurs and institute appropriate emergency care. For patients with Grade 1, 2, or 3 reactions, reduce the infusion rate when re-starting the infusion.

To reduce the risk of delayed infusion-related reactions, administer oral corticosteroids to all patients following DARZALEX[®] infusions. Patients with a history of chronic obstructive pulmonary disease may require additional post-infusion medications to manage respiratory complications. Consider prescribing short and long-acting bronchodilators and inhaled corticosteroids for patients with chronic obstructive pulmonary disease.

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 DARZALEX[®] infusion. If ocular symptoms occur, interrupt DARZALEX[®] infusion and seek immediate ophthalmologic evaluation prior to restarting DARZALEX[®].

DARZALEX FASPRO[®]: 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.

DARZALEX[®] and DARZALEX *FASPRO*[®]: Neutropenia and Thrombocytopenia

DARZALEX[®] and DARZALEX *FASPRO*[®] may increase neutropenia and thrombocytopenia 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[®] or DARZALEX *FASPRO*[®] until recovery of neutrophils or for recovery of platelets.

In lower body weight patients receiving DARZALEX *FASPRO*[®], higher rates of Grade 3-4 neutropenia were observed.

DARZALEX[®] and DARZALEX *FASPRO*[®]: 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[®] and DARZALEX *FASPRO*[®]. Type and screen patients prior to starting DARZALEX[®] and DARZALEX *FASPRO*[®].

DARZALEX[®] and 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 patients with IgG kappa myeloma protein.

DARZALEX[®] and DARZALEX *FASPRO*[®]: Embryo-Fetal Toxicity

Based on the mechanism of action, DARZALEX[®] and DARZALEX *FASPRO*[®] can cause fetal harm when administered to a pregnant woman. DARZALEX[®] and 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[®] or DARZALEX *FASPRO*[®] and for 3 months after the last dose.

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

DARZALEX[®]: ADVERSE REACTIONS

The most frequently reported adverse reactions (incidence $\geq 20\%$) were upper respiratory infection, neutropenia, infusion-related reactions, thrombocytopenia, diarrhea, constipation, anemia, peripheral sensory neuropathy, fatigue, peripheral edema, nausea, cough, pyrexia, dyspnea, and asthenia. The most common hematologic laboratory abnormalities ($\geq 40\%$) with DARZALEX[®] are neutropenia, lymphopenia, thrombocytopenia, leukopenia, and anemia.

DARZALEX *FASPRO*[®]: ADVERSE REACTIONS

In multiple myeloma, the most common adverse reaction ($\geq 20\%$) with DARZALEX *FASPRO*[®] monotherapy is upper respiratory tract infection. The most common adverse reactions with combination therapy ($\geq 20\%$ 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 hematologic laboratory abnormalities ($\geq 40\%$) with DARZALEX *FASPRO*[®] are decreased leukocytes, decreased lymphocytes, decreased neutrophils, decreased platelets, and decreased hemoglobin.

Please read full [Prescribing Information](#) for DARZALEX[®].

Please read full [Prescribing Information](#) for DARZALEX *FASPRO*[®].

CARVYKTI™ IMPORTANT SAFETY INFORMATION

INDICATIONS AND USAGE

CARVYKTI™ (ciltacabtagene autoleucel) is a B-cell maturation antigen (BCMA)-directed genetically modified autologous T cell immunotherapy indicated for the treatment of adult patients with relapsed or refractory multiple myeloma, after four or more prior lines of therapy, including a proteasome inhibitor, an immunomodulatory agent, and an anti-CD38 monoclonal antibody.

WARNING: CYTOKINE RELEASE SYNDROME, NEUROLOGIC TOXICITIES, HLH/MAS, and PROLONGED and RECURRENT CYTOPENIA

Cytokine Release Syndrome (CRS), including fatal or life-threatening reactions, occurred in patients following treatment with CARVYKTI™. Do not administer CARVYKTI™ to patients with active infection or inflammatory disorders. Treat severe or life-threatening CRS with tocilizumab or tocilizumab and corticosteroids.

Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS), which may be fatal or life-threatening, occurred following treatment with CARVYKTI™, including before CRS onset, concurrently with CRS, after CRS resolution, or in the absence of CRS. Monitor for neurologic events after treatment with CARVYKTI™. Provide supportive care and/or corticosteroids as needed.

Parkinsonism and Guillain-Barré syndrome and their associated complications resulting in fatal or life-threatening reactions have occurred following treatment with CARVYKTI™.

Hemophagocytic Lymphohistiocytosis/Macrophage Activation Syndrome (HLH/MAS), including fatal and life-threatening reactions, occurred in patients following treatment with CARVYKTI™. HLH/MAS can occur with CRS or neurologic toxicities.

Prolonged and/or recurrent cytopenias with bleeding and infection and requirement for stem cell transplantation for hematopoietic recovery occurred following treatment with CARVYKTI™.

CARVYKTI™ is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the CARVYKTI™ REMS Program.

WARNINGS AND PRECAUTIONS

Cytokine Release Syndrome (CRS) including fatal or life-threatening reactions, occurred following treatment with CARVYKTI™ in 95% (92/97) of patients receiving ciltacabtagene autoleucel. Grade 3 or higher CRS (2019 ASTCT grade) occurred in 5% (5/97) of patients, with Grade 5 CRS reported in 1 patient. The median time to onset of CRS was 7 days (range: 1-12 days). The most common manifestations of CRS included pyrexia (100%), hypotension (43%), increased aspartate aminotransferase (AST) (22%), chills (15%), increased alanine aminotransferase (14%) and sinus tachycardia (11%). Grade 3 or higher events associated with CRS included increased AST and ALT, hyperbilirubinemia, hypotension, pyrexia, hypoxia, respiratory failure, acute kidney injury, disseminated intravascular coagulation, HLH/MAS, angina pectoris, supraventricular and ventricular tachycardia, malaise, myalgias, increased C-reactive protein, ferritin, blood alkaline phosphatase and gamma-glutamyl transferase.

Identify CRS based on clinical presentation. Evaluate for and treat other causes of fever, hypoxia, and hypotension. CRS has been reported to be associated with findings of HLH/MAS, and the physiology of the syndromes may overlap. HLH/MAS is a potentially life-threatening condition. In patients with progressive symptoms of CRS or refractory CRS despite treatment, evaluate for evidence of HLH/MAS.

Sixty-nine of 97 (71%) patients received tocilizumab and/or a corticosteroid for CRS after infusion of ciltacabtagene autoleucel. Forty-four (45%) patients received only tocilizumab, of whom 33 (34%) received a single dose and 11 (11%) received more than one dose; 24 patients (25%) received tocilizumab and a corticosteroid, and one patient

(1%) received only corticosteroids. Ensure that a minimum of two doses of tocilizumab are available prior to infusion of CARVYKTI™.

Monitor patients at least daily for 10 days following CARVYKTI™ infusion at a REMS-certified healthcare facility for signs and symptoms of CRS. Monitor patients for signs or symptoms of CRS for at least 4 weeks after infusion. At the first sign of CRS, immediately institute treatment with supportive care, tocilizumab, or tocilizumab and corticosteroids. Counsel patients to seek immediate medical attention should signs or symptoms of CRS occur at any time.

Neurologic toxicities, which may be severe, life-threatening or fatal, occurred following treatment with CARVYKTI™. Neurologic toxicities included ICANS, neurologic toxicity with signs and symptoms of parkinsonism, Guillain-Barré Syndrome, peripheral neuropathies, and cranial nerve palsies. Counsel patients on the signs and symptoms of these neurologic toxicities, and on the delayed nature of onset of some of these toxicities. Instruct patients to seek immediate medical attention for further assessment and management if signs or symptoms of any of these neurologic toxicities occur at any time.

Overall, one or more subtypes of neurologic toxicity described below occurred following ciltacabtagene autoleucel in 26% (25/97) of patients, of which 11% (11/97) of patients experienced Grade 3 or higher events. These subtypes of neurologic toxicities were also observed in two ongoing studies.

Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS): Patients may experience fatal or life-threatening ICANS following treatment with CARVYKTI™, including before CRS onset, concurrently with CRS, after CRS resolution, or in the absence of CRS. ICANS occurred in 23% (22/97) of patients receiving ciltacabtagene autoleucel including Grade 3 or 4 events in 3% (3/97) and Grade 5 (fatal) events in 2% (2/97). The median time to onset of ICANS was 8 days (range 1-28 days). All 22 patients with ICANS had CRS. The most frequent ($\geq 5\%$) manifestation of ICANS included encephalopathy (23%), aphasia (8%) and headache (6%).

Monitor patients at least daily for 10 days following CARVYKTI™ infusion at the REMS-certified healthcare facility for signs and symptoms of ICANS. Rule out other causes of ICANS symptoms. Monitor patients for signs or symptoms of ICANS for at least 4 weeks

after infusion and treat promptly. Neurologic toxicity should be managed with supportive care and/or corticosteroids as needed.

Parkinsonism: Of the 25 patients in the CARTITUDE-1 study experiencing any neurotoxicity, five male patients had neurologic toxicity with several signs and symptoms of parkinsonism, distinct from immune effector cell-associated neurotoxicity syndrome (ICANS). Neurologic toxicity with parkinsonism has been reported in other ongoing trials of ciltacabtagene autoleucel. Patients had parkinsonian and non-parkinsonian symptoms that included tremor, bradykinesia, involuntary movements, stereotypy, loss of spontaneous movements, masked facies, apathy, flat affect, fatigue, rigidity, psychomotor retardation, micrographia, dysgraphia, apraxia, lethargy, confusion, somnolence, loss of consciousness, delayed reflexes, hyperreflexia, memory loss, difficulty swallowing, bowel incontinence, falls, stooped posture, shuffling gait, muscle weakness and wasting, motor dysfunction, motor and sensory loss, akinetic mutism, and frontal lobe release signs. The median onset of parkinsonism in the 5 patients in CARTITUDE-1 was 43 days (range 15-108) from infusion of ciltacabtagene autoleucel.

Monitor patients for signs and symptoms of parkinsonism that may be delayed in onset and managed with supportive care measures. There is limited efficacy information with medications used for the treatment of Parkinson's disease, for the improvement or resolution of parkinsonism symptoms following CARVYKTI™ treatment.

Guillain-Barré Syndrome: A fatal outcome following Guillain-Barré Syndrome (GBS) has occurred in another ongoing study of ciltacabtagene autoleucel despite treatment with intravenous immunoglobulins. Symptoms reported include those consistent with Miller-Fisher variant of GBS, encephalopathy, motor weakness, speech disturbances and polyradiculoneuritis.

Monitor for GBS. Evaluate patients presenting with peripheral neuropathy for GBS. Consider treatment of GBS with supportive care measures and in conjunction with immunoglobulins and plasma exchange, depending on severity of GBS.

Peripheral Neuropathy: Six patients in CARTITUDE-1 developed peripheral neuropathy. These neuropathies presented as sensory, motor or sensorimotor neuropathies. Median time of onset of symptoms was 62 days (range 4-136 days), median duration of

peripheral neuropathies was 256 days (range 2-465 days) including those with ongoing neuropathy. Patients who experienced peripheral neuropathy also experienced cranial nerve palsies or GBS in other ongoing trials of ciltacabtagene autoleucel.

Cranial Nerve Palsies: Three patients (3.1%) experienced cranial nerve palsies in CARTITUDE-1. All three patients had 7th cranial nerve palsy; one patient had 5th cranial nerve palsy as well. Median time to onset was 26 days (range 21-101 days) following infusion of ciltacabtagene autoleucel. Occurrence of 3rd and 6th cranial nerve palsy, bilateral 7th cranial nerve palsy, worsening of cranial nerve palsy after improvement, and occurrence of peripheral neuropathy in patients with cranial nerve palsy have also been reported in ongoing trials of ciltacabtagene autoleucel. Monitor patients for signs and symptoms of cranial nerve palsies. Consider management with systemic corticosteroids, depending on the severity and progression of signs and symptoms.

Hemophagocytic Lymphohistiocytosis (HLH)/Macrophage Activation Syndrome (MAS): Fatal HLH occurred in one patient (1%), 99 days after ciltacabtagene autoleucel. The HLH event was preceded by prolonged CRS lasting 97 days. The manifestations of HLH/MAS include hypotension, hypoxia with diffuse alveolar damage, coagulopathy, cytopenia, and multi-organ dysfunction, including renal dysfunction. HLH is a life-threatening condition with a high mortality rate if not recognized and treated early. Treatment of HLH/MAS should be administered per institutional standards.

CARVYKTI™ REMS: Because of the risk of CRS and neurologic toxicities, CARVYKTI™ is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the CARVYKTI™ REMS.

Further information is available at www.CARVYKTIrems.com or 1-844-672-0067.

Prolonged and Recurrent Cytopenias: Patients may exhibit prolonged and recurrent cytopenias following lymphodepleting chemotherapy and CARVYKTI™ infusion. One patient underwent autologous stem cell therapy for hematopoietic reconstitution due to prolonged thrombocytopenia.

In CARTITUDE-1, 30% (29/97) of patients experienced prolonged Grade 3 or 4 neutropenia and 41% (40/97) of patients experienced prolonged Grade 3 or 4

thrombocytopenia that had not resolved by Day 30 following ciltacabtagene autoleucel infusion.

Recurrent Grade 3 or 4 neutropenia, thrombocytopenia, lymphopenia and anemia were seen in 63% (61/97), 18% (17/97), 60% (58/97), and 37% (36/97) after recovery from initial Grade 3 or 4 cytopenia following infusion. After Day 60 following ciltacabtagene autoleucel infusion, 31%, 12% and 6% of patients had a recurrence of Grade 3 or higher lymphopenia, neutropenia and thrombocytopenia, respectively, after initial recovery of their Grade 3 or 4 cytopenia. Eighty-seven percent (84/97) of patients had one, two, or three or more recurrences of Grade 3 or 4 cytopenias after initial recovery of Grade 3 or 4 cytopenia. Six and 11 patients had Grade 3 or 4 neutropenia and thrombocytopenia, respectively, at the time of death.

Monitor blood counts prior to and after CARVYKTI™ infusion. Manage cytopenias with growth factors and blood product transfusion support according to local institutional guidelines.

Infections: CARVYKTI™ should not be administered to patients with active infection or inflammatory disorders. Severe, life-threatening or fatal infections occurred in patients after CARVYKTI™ infusion.

Infections (all grades) occurred in 57 (59%) patients. Grade 3 or 4 infections occurred in 23% (22/97) of patients; Grade 3 or 4 infections with an unspecified pathogen occurred in 17%, viral infections in 7%, bacterial infections in 1%, and fungal infections in 1% of patients. Overall, four patients had Grade 5 infections: lung abscess (n=1), sepsis (n=2) and pneumonia (n=1).

Monitor patients for signs and symptoms of infection before and after CARVYKTI™ infusion and treat patients appropriately. Administer prophylactic, pre-emptive and/or therapeutic antimicrobials according to the standard institutional guidelines. Febrile neutropenia was observed in 10% of patients after ciltacabtagene autoleucel infusion, and may be concurrent with CRS. In the event of febrile neutropenia, evaluate for infection and manage with broad-spectrum antibiotics, fluids and other supportive care, as medically indicated.

Viral Reactivation: Hepatitis B virus (HBV) reactivation, in some cases resulting in fulminant hepatitis, hepatic failure and death, can occur in patients with hypogammaglobulinemia. Perform screening for Cytomegalovirus (CMV), HBV, hepatitis C virus (HCV), and human immunodeficiency virus (HIV), or any other infectious agents if clinically indicated in accordance with clinical guidelines before collection of cells for manufacturing. Consider antiviral therapy to prevent viral reactivation per local institutional guidelines/clinical practice.

Hypogammaglobulinemia was reported as an adverse event in 12% (12/97) of patients; laboratory IgG levels fell below 500 mg/dL after infusion in 92% (89/97) of patients. Monitor immunoglobulin levels after treatment with CARVYKTI™ and administer IVIG for IgG <400 mg/dL. Manage per local institutional guidelines, including infection precautions and antibiotic or antiviral prophylaxis.

Use of Live Vaccines: The safety of immunization with live viral vaccines during or following CARVYKTI™ treatment has not been studied. Vaccination with live virus vaccines is not recommended for at least 6 weeks prior to the start of lymphodepleting chemotherapy, during CARVYKTI™ treatment, and until immune recovery following treatment with CARVYKTI™.

Hypersensitivity Reactions have occurred in 5% (5/97) of patients following ciltacabtagene autoleucel infusion. Serious hypersensitivity reactions, including anaphylaxis, may be due to the dimethyl sulfoxide (DMSO) in CARVYKTI™. Patients should be carefully monitored for 2 hours after infusion for signs and symptoms of severe reaction. Treat promptly and manage appropriately according to the severity of the hypersensitivity reaction.

Secondary Malignancies: Patients may develop secondary malignancies. Monitor life-long for secondary malignancies. In the event that a secondary malignancy occurs, contact Janssen Biotech, Inc., at 1-800-526-7736 for reporting and to obtain instructions on collection of patient samples for testing of secondary malignancy of T cell origin.

Effects on Ability to Drive and Use Machines: Due to the potential for neurologic events, including altered mental status, seizures, neurocognitive decline, or neuropathy, patients are at risk for altered or decreased consciousness or coordination in the 8 weeks

following CARVYKTI™ infusion. Advise patients to refrain from driving and engaging in hazardous occupations or activities, such as operating heavy or potentially dangerous machinery during this initial period, and in the event of new onset of any neurologic toxicities.

ADVERSE REACTIONS

The most common non-laboratory adverse reactions (incidence greater than 20%) are pyrexia, cytokine release syndrome, hypogammaglobulinemia, hypotension, musculoskeletal pain, fatigue, infections of unspecified pathogen, cough, chills, diarrhea, nausea, encephalopathy, decreased appetite, upper respiratory tract infection, headache, tachycardia, dizziness, dyspnea, edema, viral infections, coagulopathy, constipation, and vomiting. The most common laboratory adverse reactions (incidence greater than or equal to 50%) include thrombocytopenia, neutropenia, anemia, aminotransferase elevation, and hypoalbuminemia.

Please read full [Prescribing Information](#) including Boxed Warning for CARVYKTI™.

BALVERSA® IMPORTANT SAFETY INFORMATION

Warnings and Precautions

Ocular Disorders – BALVERSA® can cause ocular disorders, including central serous retinopathy/retinal pigment epithelial detachment (CSR/RPED) resulting in visual field defect.

CSR/RPED was reported in 25% of patients treated with BALVERSA®, with a median time to first onset of 50 days. Grade 3 CSR/RPED, involving central field of vision, was reported in 3% of patients. CSR/RPED resolved in 13% of patients and was ongoing in 13% of patients at the study cutoff. CSR/RPED led to dose interruptions and reductions in 9% and 14% of patients, respectively, and 3% of patients discontinued BALVERSA®. Dry eye symptoms occurred in 28% of patients during treatment with BALVERSA® and were Grade 3 in 6% of patients. All patients should receive dry eye prophylaxis with ocular demulcents as needed.

Perform monthly ophthalmological examinations during the first 4 months of treatment and every 3 months afterwards, and urgently at any time for visual symptoms. Ophthalmological examination should include assessment of visual acuity, slit lamp examination, funduscopy, and optical coherence tomography. Withhold BALVERSA® when CSR occurs and permanently discontinue if it does not resolve within 4 weeks or if Grade 4 in severity. For ocular adverse reactions, follow the dose modification guidelines [see *Dosage and Administration (2.3)*].

Hyperphosphatemia and Soft Tissue Mineralization – BALVERSA® can cause hyperphosphatemia leading to soft tissue mineralization, cutaneous calcinosis, non-uremic calciphylaxis and vascular calcification. Increases in phosphate levels are a pharmacodynamic effect of BALVERSA® [see *Pharmacodynamics (12.2)*].

Hyperphosphatemia was reported as adverse reaction in 76% of patients treated with BALVERSA®. The median onset time for any grade event of hyperphosphatemia was 20 days (range: 8–116) after initiating BALVERSA®. Thirty-two percent of patients received phosphate binders during treatment with BALVERSA®. Cutaneous calcinosis, non-uremic calciphylaxis and vascular calcification have been observed in 0.3% of patients treated with BALVERSA®.

Monitor for hyperphosphatemia throughout treatment. In all patients, restrict phosphate intake to 600-800 mg daily. If serum phosphate is above 7.0 mg/dL, consider adding an oral phosphate binder until serum phosphate level returns to <5.5 mg/dL. Withhold, dose reduce, or permanently discontinue BALVERSA® based on duration and severity of hyperphosphatemia [see *Dosage and Administration (2.3)*, *Table 2: Dose Modifications for Adverse Reactions*].

Embryo-fetal Toxicity – Based on the mechanism of action and findings in animal reproduction studies, BALVERSA® can cause fetal harm when administered to a pregnant woman. In a rat embryo-fetal toxicity study, erdafitinib was embryotoxic and teratogenic at exposures less than the human exposures at all doses studied. Advise pregnant women of the potential risk to the fetus. Advise female patients of reproductive potential to use effective contraception during treatment with BALVERSA® and for one month after the last dose. Advise male patients with female partners of reproductive potential to use

effective contraception during treatment with BALVERSA® and for one month after the last dose [see *Use in Specific Populations (8.1, 8.3)* and *Clinical Pharmacology (12.1)*].

Most common adverse reactions including laboratory abnormalities ≥20%:

Phosphate increased (76%), stomatitis (56%), fatigue (54%), creatinine increased (52%), diarrhea (47%), dry mouth (45%), onycholysis (41%), alanine aminotransferase increased (41%), alkaline phosphatase increased (41%), sodium decreased (40%), decreased appetite (38%), albumin decreased (37%), dysgeusia (37%), hemoglobin decreased (35%), dry skin (34%), aspartate aminotransferase increased (30%), magnesium decreased (30%), dry eye (28%), alopecia (26%), palmar-plantar erythrodysesthesia syndrome (26%), constipation (28%), phosphate decreased (24%), abdominal pain (23%), calcium increased (22%), nausea (21%), and musculoskeletal pain (20%). The most common Grade 3 or greater adverse reactions (>1%) were stomatitis (9%), nail dystrophy*, palmar-plantar erythrodysesthesia syndrome (6%), paronychia (3%), nail disorder*, keratitis[†], onycholysis* (10%), and hyperphosphatemia.

*Included within onycholysis. [†]Included within dry eye.

- An adverse reaction with a fatal outcome in 1% of patients was acute myocardial infarction.
- Serious adverse reactions occurred in 41% of patients, including eye disorders (10%).
- Permanent discontinuation due to an adverse reaction occurred in 13% of patients. The most frequent reasons for permanent discontinuation included eye disorders (6%).
- Dosage interruptions occurred in 68% of patients. The most frequent adverse reactions requiring dosage interruption included hyperphosphatemia (24%), stomatitis (17%), eye disorders (17%), and palmar-plantar erythrodysesthesia syndrome (8%).
- Dose reductions occurred in 53% of patients. The most frequent adverse reactions for dose reductions included eye disorders (23%), stomatitis (15%), hyperphosphatemia (7%), palmar-plantar erythrodysesthesia syndrome (7%), paronychia (7%), and nail dystrophy (6%).

Drug Interactions

- Moderate CYP2C9 or strong CYP3A4 Inhibitors: Consider alternative agents or monitor closely for adverse reactions. (7.1)
- Strong CYP2C9 or CYP3A4 inducers: Avoid concomitant use with BALVERSA®. (7.1)
- Moderate CYP2C9 or CYP3A4 inducers: Increase BALVERSA® dose up to 9 mg. (7.1)
- Serum phosphate level-altering agents: Avoid concomitant use with agents that can alter serum phosphate levels before the initial dose modification period. (2.3, 7.1)
- CYP3A4 substrates: Avoid concomitant use with sensitive CYP3A4 substrates with narrow therapeutic indices. (7.2)
- OCT2 substrates: Consider alternative agents or consider reducing the dose of OCT2 substrates based on tolerability. (7.2)
- P-gp substrates: Separate BALVERSA® administration by at least 6 hours before or after administration of P-gp substrates with narrow therapeutic indices. (7.2)

Use in Specific Populations

Lactation – Because of the potential for serious adverse reactions from erdafitinib in a breastfed child, advise lactating women not to breastfeed during treatment with BALVERSA® and for one month following the last dose.

Please see the full [Prescribing Information](#) for BALVERSA®.

RYBREVANT® IMPORTANT SAFETY INFORMATION¹⁷

WARNINGS AND PRECAUTIONS

Infusion Related Reactions¹⁷

RYBREVANT® can cause infusion related reactions (IRR); signs and symptoms of IRR include dyspnea, flushing, fever, chills, nausea, chest discomfort, hypotension, and vomiting.

Based on the safety population, IRR occurred in 66% of patients treated with RYBREVANT®. Among patients receiving treatment on Week 1 Day 1, 65% experienced an IRR, while the incidence of IRR was 3.4% with the Day 2 infusion, 0.4% with the Week 2 infusion, and cumulatively 1.1% with subsequent infusions. Of the reported IRRs, 97%

were Grade 1-2, 2.2% were Grade 3, and 0.4% were Grade 4. The median time to onset was 1 hour (range 0.1 to 18 hours) after start of infusion. The incidence of infusion modifications due to IRR was 62% and 1.3% of patients permanently discontinued RYBREVANT® due to IRR.

Premedicate with antihistamines, antipyretics, and glucocorticoids and infuse RYBREVANT® as recommended. Administer RYBREVANT® via a peripheral line on Week 1 and Week 2. Monitor patients for any signs and symptoms of infusion reactions during RYBREVANT® infusion in a setting where cardiopulmonary resuscitation medication and equipment are available. Interrupt infusion if IRR is suspected. Reduce the infusion rate or permanently discontinue RYBREVANT® based on severity.

Interstitial Lung Disease/Pneumonitis¹⁷

RYBREVANT® can cause interstitial lung disease (ILD)/pneumonitis. Based on the safety population, ILD/pneumonitis occurred in 3.3% of patients treated with RYBREVANT®, with 0.7% of patients experiencing Grade 3 ILD/pneumonitis. Three patients (1%) discontinued RYBREVANT® due to ILD/pneumonitis.

Monitor patients for new or worsening symptoms indicative of ILD/pneumonitis (e.g., dyspnea, cough, fever). Immediately withhold RYBREVANT® in patients with suspected ILD/pneumonitis and permanently discontinue if ILD/pneumonitis is confirmed.

Dermatologic Adverse Reactions¹⁷

RYBREVANT® can cause rash (including dermatitis acneiform), pruritus and dry skin. Based on the safety population, rash occurred in 74% of patients treated with RYBREVANT®, including Grade 3 rash in 3.3% of patients. The median time to onset of rash was 14 days (range: 1 to 276 days). Rash leading to dose reduction occurred in 5% of patients, and RYBREVANT® was permanently discontinued due to rash in 0.7% of patients.

Toxic epidermal necrolysis occurred in one patient (0.3%) treated with RYBREVANT®.

Instruct patients to limit sun exposure during and for 2 months after treatment with RYBREVANT®. Advise patients to wear protective clothing and use broad spectrum UVA/UVB sunscreen. Alcohol free emollient cream is recommended for dry skin.

If skin reactions develop, start topical corticosteroids and topical and/or oral antibiotics. For Grade 3 reactions, add oral steroids and consider dermatologic consultation. Promptly refer patients presenting with severe rash, atypical appearance or distribution, or lack of improvement within 2 weeks to a dermatologist. Withhold, dose reduce or permanently discontinue RYBREVANT® based on severity.

Ocular Toxicity¹⁷

RYBREVANT® can cause ocular toxicity including keratitis, dry eye symptoms, conjunctival redness, blurred vision, visual impairment, ocular itching, and uveitis. Based on the safety population, keratitis occurred in 0.7% and uveitis occurred in 0.3% of patients treated with RYBREVANT®. All events were Grade 1-2. Promptly refer patients presenting with eye symptoms to an ophthalmologist. Withhold, dose reduce or permanently discontinue RYBREVANT® based on severity.

Embryo Fetal Toxicity¹⁷

Based on its mechanism of action and findings from animal models, RYBREVANT® can cause fetal harm when administered to a pregnant woman. Advise females of reproductive potential of the potential risk to the fetus. Advise female patients of reproductive potential to use effective contraception during treatment and for 3 months after the final dose of RYBREVANT®.

Adverse Reactions¹⁷

The most common adverse reactions ($\geq 20\%$) were rash (84%), IRR (64%), paronychia (50%), musculoskeletal pain (47%), dyspnea (37%), nausea (36%), fatigue (33%), edema (27%), stomatitis (26%), cough (25%), constipation (23%), and vomiting (22%). The most common Grade 3 to 4 laboratory abnormalities ($\geq 2\%$) were decreased lymphocytes (8%), decreased albumin (8%), decreased phosphate (8%), decreased potassium (6%), increased alkaline phosphatase (4.8%), increased glucose (4%), increased gamma-glutamyl transferase (4%), and decreased sodium (4%).

Please read full [Prescribing Information](#) for RYBREVANT®.

ERLEADA® IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

Cerebrovascular and Ischemic Cardiovascular Events — In a randomized study (SPARTAN) of patients with nmCRPC, ischemic cardiovascular events occurred in 3.7% of patients treated with ERLEADA® and 2% of patients treated with placebo. In a randomized study (TITAN) in patients with mCSPC, ischemic cardiovascular events occurred in 4.4% of patients treated with ERLEADA® and 1.5% of patients treated with placebo. Across the SPARTAN and TITAN studies, 4 patients (0.3%) treated with ERLEADA® and 2 patients (0.2%) treated with placebo died from an ischemic cardiovascular event. Patients with history of unstable angina, myocardial infarction, congestive heart failure, stroke, or transient ischemic attack within 6 months of randomization were excluded from the SPARTAN and TITAN studies.

In the SPARTAN study, cerebrovascular events occurred in 2.5% of patients treated with ERLEADA® and 1% of patients treated with placebo. In the TITAN study, cerebrovascular events occurred in 1.9% of patients treated with ERLEADA® and 2.1% of patients treated with placebo. Across the SPARTAN and TITAN studies, 3 patients (0.2%) treated with ERLEADA®, and 2 patients (0.2%) treated with placebo died from a cerebrovascular event.

Cerebrovascular and ischemic cardiovascular events, including events leading to death, occurred in patients receiving ERLEADA®. Monitor for signs and symptoms of ischemic heart disease and cerebrovascular disorders. Optimize management of cardiovascular risk factors, such as hypertension, diabetes, or dyslipidemia. Consider discontinuation of ERLEADA® for Grade 3 and 4 events.

Fractures — In a randomized study (SPARTAN) of patients with nmCRPC, fractures occurred in 12% of patients treated with ERLEADA® and in 7% of patients treated with placebo. In a randomized study (TITAN) of patients with mCSPC, fractures occurred in 9% of patients treated with ERLEADA® and in 6% of patients treated with placebo. Evaluate patients for fracture risk. Monitor and manage patients at risk for fractures according to established treatment guidelines and consider use of bone-targeted agents.

Falls — In a randomized study (SPARTAN), falls occurred in 16% of patients treated with ERLEADA[®] compared with 9% of patients treated with placebo. Falls were not associated with loss of consciousness or seizure. Falls occurred in patients receiving ERLEADA[®] with increased frequency in the elderly. Evaluate patients for fall risk.

Seizure — In two randomized studies (SPARTAN and TITAN), 5 patients (0.4%) treated with ERLEADA[®] and 1 patient treated with placebo (0.1%) experienced a seizure. Permanently discontinue ERLEADA[®] in patients who develop a seizure during treatment. It is unknown whether anti-epileptic medications will prevent seizures with ERLEADA[®]. Advise patients of the risk of developing a seizure while receiving ERLEADA[®] and of engaging in any activity where sudden loss of consciousness could cause harm to themselves or others.

Embryo-Fetal Toxicity — The safety and efficacy of ERLEADA[®] have not been established in females. Based on findings from animals and its mechanism of action, ERLEADA[®] can cause fetal harm and loss of pregnancy when administered to a pregnant female. Advise males with female partners of reproductive potential to use effective contraception during treatment and for 3 months after the last dose of ERLEADA[®] [see *Use in Specific Populations (8.1, 8.3)*].

ADVERSE REACTIONS

The most common adverse reactions ($\geq 10\%$) that occurred more frequently in the ERLEADA[®]-treated patients ($\geq 2\%$ over placebo) from the randomized placebo-controlled clinical trials (TITAN and SPARTAN) were fatigue, arthralgia, rash, decreased appetite, fall, weight decreased, hypertension, hot flush, diarrhea, and fracture.

Laboratory Abnormalities — All Grades (Grade 3-4)

- **Hematology** — In the TITAN study: white blood cell decreased ERLEADA[®] 27% (0.4%), placebo 19% (0.6%). In the SPARTAN study: anemia ERLEADA[®] 70% (0.4%), placebo 64% (0.5%); leukopenia ERLEADA[®] 47% (0.3%), placebo 29% (0%); lymphopenia ERLEADA[®] 41% (1.8%), placebo 21% (1.6%)
- **Chemistry** — In the TITAN study: hypertriglyceridemia ERLEADA[®] 17% (2.5%), placebo 12% (2.3%). In the SPARTAN study: hypercholesterolemia ERLEADA[®] 76% (0.1%), placebo 46% (0%); hyperglycemia ERLEADA[®] 70% (2%), placebo 59%

(1.0%); hypertriglyceridemia ERLEADA® 67% (1.6%), placebo 49% (0.8%); hyperkalemia ERLEADA® 32% (1.9%), placebo 22% (0.5%)

- **Rash** — In 2 randomized studies (SPARTAN and TITAN), rash was most commonly described as macular or maculopapular. Adverse reactions of rash were 26% with ERLEADA® vs 8% with placebo. Grade 3 rashes (defined as covering >30% body surface area [BSA]) were reported with ERLEADA® treatment (6%) vs placebo (0.5%).

The onset of rash occurred at a median of 83 days. Rash resolved in 78% of patients within a median of 78 days from onset of rash. Rash was commonly managed with oral antihistamines, topical corticosteroids, and 19% of patients received systemic corticosteroids. Dose reduction or dose interruption occurred in 14% and 28% of patients, respectively. Of the patients who had dose interruption, 59% experienced recurrence of rash upon reintroduction of ERLEADA®.

Hypothyroidism — In 2 randomized studies (SPARTAN and TITAN), hypothyroidism was reported for 8% of patients treated with ERLEADA® and 1.5% of patients treated with placebo based on assessments of thyroid-stimulating hormone (TSH) every 4 months. Elevated TSH occurred in 25% of patients treated with ERLEADA® and 7% of patients treated with placebo. The median onset was at the first scheduled assessment. There were no Grade 3 or 4 adverse reactions. Thyroid replacement therapy, when clinically indicated, should be initiated or dose-adjusted.

DRUG INTERACTIONS

Effect of Other Drugs on ERLEADA® — Co-administration of a strong CYP2C8 or CYP3A4 inhibitor is predicted to increase the steady-state exposure of the active moieties. No initial dose adjustment is necessary; however, reduce the ERLEADA® dose based on tolerability [*see Dosage and Administration (2.2)*].

Effect of ERLEADA® on Other Drugs

CYP3A4, CYP2C9, CYP2C19, and UGT Substrates — ERLEADA® is a strong inducer of CYP3A4 and CYP2C19, and a weak inducer of CYP2C9 in humans. Concomitant use of ERLEADA® with medications that are primarily metabolized by CYP3A4, CYP2C19, or CYP2C9 can result in lower exposure to these medications. Substitution for these medications is recommended when possible or evaluate for loss of activity if medication

is continued. Concomitant administration of ERLEADA[®] with medications that are substrates of UDP-glucuronosyl transferase (UGT) can result in decreased exposure. Use caution if substrates of UGT must be co-administered with ERLEADA[®] and evaluate for loss of activity.

P-gp, BCRP, or OATP1B1 Substrates — Apalutamide is a weak inducer of P-glycoprotein (P-gp), breast cancer resistance protein (BCRP), and organic anion transporting polypeptide 1B1 (OATP1B1) clinically. Concomitant use of ERLEADA[®] with medications that are substrates of P-gp, BCRP, or OATP1B1 can result in lower exposure of these medications. Use caution if substrates of P-gp, BCRP, or OATP1B1 must be co-administered with ERLEADA[®] and evaluate for loss of activity if medication is continued.

Please see the full [Prescribing Information](#) for ERLEADA[®].

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At Janssen, we're creating a future where disease is a thing of the past. We're the Pharmaceutical Companies of Johnson & Johnson, working tirelessly to make that future a reality for patients everywhere by fighting sickness with science, improving access with ingenuity, and healing hopelessness with heart. We focus on areas of medicine where we can make the biggest difference: Cardiovascular, Metabolism & Retina; Immunology; Infectious Diseases & Vaccines; Neuroscience; Oncology; and Pulmonary Hypertension.

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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 and the potential benefits and treatment impact of IMBRUVICA[®] (ibrutinib), DARZALEX[®] (daratumumab), DARZALEX FASPRO[®] (daratumumab and hyaluronidase-fihj), CARVYKTI[™] (ciltacabtagene autoleucel), teclistamab, talquetamab, BALVERSA[®] (erdafitinib), RYBREVANT[®]

(amivantamab-vmjw), niraparib and ERLEADA® (apalutamide). 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 or any of the other Janssen Pharmaceutical Companies 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; manufacturing difficulties and delays; competition, including technological advances, new products and patents attained by competitors; challenges to patents; product efficacy or safety concerns resulting in product recalls or regulatory action; 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 2, 2022, including in the sections captioned "Cautionary Note Regarding Forward-Looking Statements" and "Item 1A. Risk Factors," and in Johnson & Johnson's subsequent 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 the Janssen Pharmaceutical Companies nor Johnson & Johnson undertakes to update any forward-looking statement as a result of new information or future events or developments.

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