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For immediate release

Johnson & Johnson advances leadership in oncology innovation with more than 75 clinical study and real-world presentations at ASCO and EHA

PALOMA-3 presentation of subcutaneous amivantamab and lazertinib selected to showcase cutting-edge approaches in lung cancer during prestigious "Best of ASCO" program

New data showcase first- and -best-in-class, complementary multiple myeloma therapies, including DARZALEX® (daratumumab), CARVYKTI® (ciltacabtagene autoleucel; cilta-cel), TECVAYLI® (teclistamab-cqyv) and TALVEY® (talquetamab-tgvs)

RARITAN, N.J., May 23, 2024 – Johnson & Johnson announced today that the 2024 American Society of Clinical Oncology (ASCO) Annual Meeting will feature 34 clinical study and real-world evidence presentations from the Company's hematologic malignancies and solid tumor oncology product portfolio and pipeline. Additionally, 43 abstracts will be presented at the European Hematology Association (EHA) 2024 Congress the following week. Eighteen oral presentations across both meetings include new data from pivotal trials and updated clinical data in lung cancer, prostate cancer, bladder cancer, multiple myeloma, and B-cell and myeloid malignancies.

"Our data at ASCO and EHA this year demonstrate our long-standing commitment to advance the treatment of solid tumors and blood cancers with the goal of transforming outcomes for those who battle with these complex diseases," said Yusri Elsayed, M.D., M.H.Sc., Ph.D., Global Therapeutic Head, Oncology, Johnson & Johnson Innovative Medicine. "With a legacy in oncology innovation spanning three decades, our mission to redefine the standard of care in hematologic malignancies and solid tumors has never been stronger as we work every day to get in front of cancer."

"With nearly 20 million people diagnosed annually worldwide, we innovate with purpose to lead where medicine is going and ultimately transform outcomes for people living with cancer," said Biljana Naumovic, U.S. President, Oncology, Solid Tumor, Johnson & Johnson Innovative Medicine. "This year, we look forward to presenting data that represent our commitment to unlocking the value of innovation in treatment across a range of difficult-to-treat cancers, disease stages and risk factors for patients who have limited options."

Key Data Presentations

Lung Cancer at ASCO

- Late-breaking results from the Phase 3 PALOMA-3 study evaluating **subcutaneous amivantamab** combined with **lazertinib** in patients with non-small cell lung cancer (NSCLC) with epidermal growth factor receptor (*EGFR*) exon 19 deletion (ex19del) or L858R mutations (Oral Abstract #LBA8505)
- Data from the Phase 2 PALOMA-2 study evaluating **subcutaneous amivantamab** combined with **lazertinib** as first-line treatment in patients with advanced NSCLC with *EGFR* ex19del or L858R mutations (Poster Abstract #LBA8612)

- Subgroup analysis from the landmark Phase 3 MARIPOSA study evaluating first-line treatment with **RYBREVANT®** (amivantamab-vmjw) and **lazertinib** in patients exhibiting high-risk clinical and biological features commonly observed in *EGFR*-mutant advanced NSCLC, who typically experience poorer outcomes (Oral Abstract #8504)
- Results from Cohort C of the CHRYSALIS-2 study evaluating **RYBREVANT®** plus **lazertinib** in patients with atypical *EGFR*-mutant advanced NSCLC who were treatment-naïve or received two or fewer prior lines of treatment (Oral Abstract #8516)

Prostate Cancer at ASCO

- First presentation of data from the first-in-human Phase 1 study evaluating **JNJ-69086420**, a first-in-class radioligand therapy, targeting human kallikrein 2 (hK2) with an actinium-225 (^{225}Ac)-labeled antibody to treat patients with metastatic castration-resistant prostate cancer (Oral Abstract #5010)

Bladder Cancer at ASCO

- An analysis of fibroblast growth factor receptor (*FGFR*) alterations in patients who develop locally advanced metastatic urothelial cancer (mUC) and their association with tumor subtype and clinical outcomes in patients treated with **BALVERSA®** (erdafitinib) versus pembrolizumab (Poster Abstract #4578)

Multiple Myeloma at ASCO and EHA

ASCO Highlights

- Additional analyses from the Phase 3 PERSEUS study assessing the impact of **DARZALEX *FASPRO*®** (daratumumab and hyaluronidase-fihj) for induction and consolidation treatment and maintenance therapy on deepening minimal residual disease (MRD) response, sustained MRD and progression-free survival based on reaching MRD in patients who are transplant-eligible with newly diagnosed multiple myeloma (Oral Abstract #7502)
- Analysis of data from the Phase 3 CARTITUDE-4 study of **CARVYKTI®** (ciltacabtagene autoleucel; cilta-cel) investigating the subgroup of patients with functional high-risk multiple myeloma treated with **CARVYKTI®** as second-line therapy (Oral Abstract #7504)
- Results from the Phase 2 CARTITUDE-2 Cohort D study of **CARVYKTI®** investigating the efficacy and safety of **CARVYKTI®** with lenalidomide maintenance in patients with suboptimal response to frontline autologous stem cell transplant (Oral Abstract #7505)
- Updated analysis with longer-term follow-up from the Phase 1/2 MajesTEC-1 study of **TECVAYLI®** in patients with relapsed or refractory multiple myeloma receiving prophylactic tocilizumab for the reduction of cytokine release syndrome (Oral Abstract #7517)
- Long-term follow-up data from the Phase 1/2 MajesTEC-1 study of **TECVAYLI®** in patients with relapsed or refractory multiple myeloma (Poster Abstract #7540)
- First data from safety run in from the Phase 3 MajesTEC-7 study of **TECVAYLI®** in patients with transplant ineligible/not intended newly diagnosed multiple myeloma (Oral Abstract #7506)
- First data from the Phase 2 OPTec study evaluating outpatient step-up administration of **TECVAYLI®** using prophylactic tocilizumab in patients with relapsed or refractory multiple myeloma (Poster Abstract #7528)

EHA Highlights

- Data from the Phase 3 PERSEUS study assessing the impact of **DARZALEX *FASPRO*®** (daratumumab and hyaluronidase-fihj) for induction and consolidation treatment and maintenance therapy on deepening minimal residual disease (MRD) response, sustained MRD and progression-free survival based on reaching MRD in patients who are transplant-eligible with newly diagnosed multiple myeloma (Oral Abstract #S201)

- Final overall survival analysis from the Phase 3 MAIA study evaluating **DARZALEX®** plus lenalidomide and dexamethasone compared to lenalidomide and dexamethasone in transplant-ineligible patients with newly diagnosed multiple myeloma (Poster Abstract #P968)
- Six-year follow-up data from the Phase 3 CASSIOPEIA study evaluating **DARZALEX®** in combination with bortezomib, thalidomide and dexamethasone (D-VTd) followed by an every 8 week **DARZALEX®** maintenance regimen in transplant-eligible, newly diagnosed multiple myeloma (Oral Abstract #S204)
- Long-term efficacy and safety results from the Phase 1/2 MonumenTAL-1 study of **TALVEY®** (talquetamab-tgvs) in patients with relapsed/refractory multiple myeloma (Poster Abstract #P915)
- Safety and efficacy results from the Phase 1b MonumenTAL-2 study evaluating **TALVEY®** in combination with pomalidomide in patients with relapsed/refractory multiple myeloma (Poster Abstract #P911)
- Results from the MajesTEC-1 study evaluating **TECVAYLI®** in patients with high-risk relapsed or refractory multiple myeloma, and the clinical benefit and durability of **TECVAYLI®** (Poster Abstract #P923)

B-Cell Malignancies at ASCO and EHA

ASCO Highlights

- Outcomes in high-risk subgroups after 5.5 years of follow-up from the Phase 2 CAPTIVATE study evaluating fixed-duration **IMBRUVICA®** (ibrutinib) plus venetoclax in patients with chronic lymphocytic leukemia (CLL) and small lymphocytic lymphoma (SLL) (Oral Abstract #7009)
- Efficacy and safety results from the Phase 3 SYMPATICO study of **IMBRUVICA®** plus venetoclax in patients with mantle cell lymphoma (MCL) and TP53 mutations (Oral Abstract #7007)

EHA Highlights

- Ten-year follow-up data from the Phase 3 RESONATE-2 study evaluating first-line **IMBRUVICA®** treatment in patients with CLL/SLL (Poster Abstract #P670)
- Presentation of outcomes in high-risk subgroups after 5.5 years of follow-up from the Phase 2 CAPTIVATE study evaluating fixed-duration **IMBRUVICA®** plus venetoclax in patients with CLL/SLL (Poster Abstract #P675)
- Comparison of overall survival between patients with CLL treated with first-line **IMBRUVICA®** to an age-matched European population (Poster Abstract #P664)
- Presentation of efficacy and safety results from the Phase 3 SYMPATICO study of **IMBRUVICA®** plus venetoclax in patients with MCL and TP53 mutations (Poster Abstract #P1128)

Myeloid Malignancies at EHA

- Data from the Phase 1b study of the Menin-KMT2a inhibitor JNJ-75276617 in combination with venetoclax and azacitidine in patients with relapsed or refractory acute myeloid leukemia harboring certain genetic alterations (Oral Abstract #S133)

Warm Autoimmune Hemolytic Anemia at EHA

- Data from a real-world longitudinal population-based study reporting on overall survival and the use of conventional treatments, including corticosteroids and immunosuppressants, in Swedish patients with primary or secondary warm Autoimmune Hemolytic Anemia (wAIHA) (Poster Abstract # P1545)

Johnson & Johnson presentations at ASCO 2024 Annual Meeting:

Lung Cancer

Oral Presentations	
Abstract #8504	Amivantamab plus lazertinib vs osimertinib in first-line *EGFR*-mutant advanced non-small cell lung cancer (NSCLC) with biomarkers of high-risk disease: A secondary analysis from the Phase 3 MARIPOSA study
Abstract #LBA8505	Subcutaneous amivantamab vs intravenous amivantamab, both in combination with lazertinib, in refractory *EGFR*-mutated, advanced NSCLC: Primary results, including overall survival (OS), from the global, Phase 3, randomized controlled PALOMA-3 trial
Abstract #8516	Amivantamab plus lazertinib in atypical *EGFR*-mutated advanced NSCLC: Results from CHRYSALIS-2
Poster Presentations	
Abstract #LBA8612	Subcutaneous amivantamab and lazertinib as first-line treatment in patients with *EGFR*-mutated, advanced NSCLC: Results from the Phase 2 PALOMA-2 study
Abstract #8619	Amivantamab plus capmatinib in advanced NSCLC harboring MET alterations: Identification of the recommended Phase 2 combination dose and preliminary dose-escalation results from the Phase 1/2 METalmark study
Abstract #8606	Amivantamab plus chemotherapy vs. chemotherapy as first-line treatment among patients with *EGFR* exon 20 insertion–mutated advanced NSCLC: PAPILLON Chinese subgroup analysis
Prostate Cancer	
Oral Presentations	
Abstract #5010	A Phase 1 study of JNJ-69086420 (JNJ-6420), an actinium-225 (^{225}Ac)-labeled antibody targeting human kallikrein 2 (hk2) to treat metastatic castration-resistant prostate cancer (mCRPC)
Poster Presentations	
Abstract #5076	Rapid and deep prostate-specific antigen (PSA) response to apalutamide plus androgen deprivation therapy (ADT) and survival in metastatic castration-sensitive prostate cancer (mCSPC) in real-world practice in the US (OASIS Project)
Abstract #5095	Clinical characteristics and treatment patterns of patients with high-risk localized prostate cancer (HR LPC) treated with radical prostatectomy (RP) and perioperative hormonal therapy (HT) in Japan, South Korea, and Taiwan
Abstract #5065	Development of a machine learning model to predict OS results from randomized clinical trials of patients with metastatic prostate cancer
Abstract #5027	PHAROS, a real-world multi-country European study on patients with high-risk localized and locally advanced prostate cancer receiving radical treatment
Abstract #11061	Prospective iterative data visualization study to enhance health literacy in prostate cancer (PC)
Abstract #TPS5119	LIBERTAS: A degendered and transgender-inclusive Phase 3 study of apalutamide (APA) plus intermittent vs continuous ADT in participants (pts) with metastatic hormone-sensitive prostate cancer (mHSPC)
Bladder Cancer	
Poster Presentation	
Abstract #4578	*FGFR3* alterations in patients who develop locally advanced or mUC, and their association with tumor subtype and clinical outcomes in patients treated with erdafitinib vs. pembrolizumab
Tumor Agnostic Disease	
Oral Presentations	
Abstract #8515	Efficacy and safety of erdafitinib in adults with NSCLC and prespecified *FGFR* alterations in the Phase 2 open-label, single-arm RAGNAR trial
Abstract #10002	Efficacy and safety of erdafitinib in pediatric patients with advanced solid tumors and *FGFR* alterations in the Phase 2 RAGNAR trial
Poster Presentations	

Abstract #1088	Efficacy and safety of erdafitinib in adults with breast cancer and prespecified *FGFR* alterations in the Phase 2 open-label, single-arm RAGNAR Trial
Abstract #3119	Efficacy of erdafitinib in adults with advanced solid tumors and non-prespecified *FGFR* mutations in the Phase 2 RAGNAR trial: Exploratory cohort
Abstract #4121	Efficacy and safety of erdafitinib in patients with advanced or metastatic cholangiocarcinoma and *FGFR* alterations: Pooled analysis of RAGNAR and LUC2001 studies
Other Solid	
Oral Presentation	
Abstract #1020	ACE-Breast-02: A pivotal Phase 2/3 trial of ARX788, a novel anti-HER2 antibody-drug conjugate (ADC), versus lapatinib plus capecitabine for HER2+ advanced breast cancer (ABC)
Poster Presentations	
Abstract #TPS1123	ACE-BREAST-03: A Phase 2 trial evaluating ARX788, an anti-HER2 antibody drug conjugate (ADC), for the treatment of HER2+ metastatic breast cancer (MBC) in patients who have been previously treated with trastuzumab deruxtecan (T-DXd)
Multiple Myeloma	
Oral Presentations	
Abstract #7502	Daratumumab plus bortezomib/lenalidomide/dexamethasone (VRD) in transplant-eligible patients with NDMM: analysis of minimal residual disease (MRD) in the PERSEUS trial
Abstract #7504	Ciltacabtagene autoleucel vs. standard of care in patients with functional high-risk multiple myeloma: CARTITUDE-4 subgroup analysis
Abstract #7505	Efficacy and safety of ciltacabtagene autoleucel ± lenalidomide maintenance in newly diagnosed multiple myeloma with suboptimal response to frontline autologous stem cell transplant: CARTITUDE-2 cohort D
Abstract #7506	Safety results from the Phase 3 MajesTEC-7 study in patients with transplant-ineligible/not intended NDMM
Abstract #7517	Longer-term follow-up of patients receiving prophylactic tocilizumab (toci) for the reduction of cytokine release syndrome (CRS) in the Phase 1/2 MajesTEC-1 study of teclistamab in relapsed/refractory multiple myeloma (RRMM)
Poster Presentations	
Abstract #7528	OPTec: A Phase 2 study to evaluate outpatient (OP) step-up administration of teclistamab, a B-cell maturation antigen (BCMA)-targeting bispecific antibody, in patients with RRMM
Abstract #7535	Ciltacabtagene autoleucel in patients with lenalidomide-refractory multiple myeloma: CARTITUDE-2 cohort A expansion subgroup
Abstract #7536	Real-world schedule de-escalation of teclistamab in patients with relapsed/refractory multiple myeloma
Abstract #7540	Long-term follow-up from the Phase 1/2 MajesTEC-1 trial of teclistamab in patients with RRMM
Abstract #7570	Clinical outcomes of retreatment with daratumumab-based regimens in anti-CD38 refractory multiple myeloma
Abstract #TPS7575	A Phase III, randomized study of daratumumab, cyclophosphamide, bortezomib and dexamethasone (DARA-VCD) induction followed by autologous stem cell transplant or DARA-VCD consolidation and daratumumab maintenance in patients with newly diagnosed AL amyloidosis
B-Cell Malignancies	
Oral Presentations	
Abstract #7007	Efficacy and safety of ibrutinib plus venetoclax in patients with mantle cell lymphoma (MCL) and TP53 mutations in the SYMPATICO study
Abstract #7009	Outcomes in high-risk subgroups after fixed-duration ibrutinib plus venetoclax for CLL/SLL: up to 5.5 years of follow-up in the Phase 2 CAPTIVATE study

Johnson & Johnson presentations at EHA 2024 Congress:

Multiple Myeloma	
Oral Presentations	
Abstract #S201	Daratumumab plus bortezomib/lenalidomide/dexamethasone in transplant-eligible patients with NDMM: analysis of MRD in the PERSEUS trial
Abstract #S204	Daratumumab (DARA) plus bortezomib/thalidomide/dexamethasone (D-VTd) followed by DARA maintenance in transplant-eligible NDMM: >6-year update of CASSIOPEIA
Abstract #S205	Ciltacabtagene autoleucel ± lenalidomide maintenance in NDMM with suboptimal response to frontline autologous stem cell transplant: CARTITUDE-2 cohort D
Poster Presentations	
Abstract #P902	Real-world schedule de-escalation of teclistamab in patients with RRMM
Abstract #P911	Talquetamab, a GPRC5D×CD3 Bispecific Antibody, in combination with pomalidomide in patients with RRMM: safety and efficacy results from the hase 1b MonumenTAL-2 study
Abstract #P913	Real-life outcomes in patients with BCMA-exposed RRMM treated with standard of care in the LocoMMotion and MoMMent studies
Abstract #P915	Long-term efficacy and safety results from the Phase 1/2 MonumenTAL-1 study of talquetamab, a GPRC5D×CD3 Bispecific Antibody, in patients with RRMM
Abstract #P920	Safety results from the Phase 3 MajesTEC-7 study in patients with transplant-ineligible/not intended NDMM
Abstract #P922	Outcomes of patients with extramedullary disease and RRMM from historical clinical trials
Abstract #P923	Efficacy and safety of teclistamab in patients with RRMM with high-risk features: a subgroup analysis from the Phase 1/2 MajesTEC-1 study
Abstract #P934	Longer-term follow-up of patients receiving prophylactic tocilizumab for reduction of cytokine release syndrome in the Phase 1/2 MajesTEC-1 study of teclistamab in RRMM
Abstract #942	Long-term follow-up from the Phase 1/2 MajesTEC-1 trial of teclistamab in patients with RRMM
Abstract #P953	Efficacy and safety of daratumumab monotherapy in newly diagnosed patients with stage 3B light-chain amyloidosis: A Phase 2 study by the European Myeloma Network
Abstract #P959	Ciltacabtagene autoleucel vs standard of care in patients with functional high-risk multiple myeloma: CARTITUDE-4 subgroup analysis
Abstract #P863	Clinical biomarkers associated with progression free survival to ciltacabtagene autoleucel in Chinese patients with RRMM from CARTIFAN-1
Abstract #P967	Comparative effectiveness of ciltacabtagene autoleucel from the CARTITUDE-4 trial vs real-world physician's choice of therapy from the flatiron registry in lenalidomide-refractory multiple myeloma
Abstract #P968	Final survival analysis of daratumumab plus lenalidomide and dexamethasone versus lenalidomide and dexamethasone in transplant-ineligible patients with NDMM: MAIA study
Abstract #P974	Daratumumab plus bortezomib/lenalidomide/dexamethasone (D-VRd) with d-r maintenance in transplant-eligible NDMM: Analysis of PERSEUS based on cytogenetic risk
Abstract #P978	Ciltacabtagene autoleucel vs standard of care in lenalidomide-refractory multiple myeloma: Phase 3 CARTITUDE-4 subgroup analysis by cytogenetic risk

Abstract #P990	Real-World Schedule De-Escalation of Teclistamab in Patients With Relapsed or Refractory Multiple Myeloma – A US National Healthcare Claims Analysis
Abstract #P992	Teclistamab step-up dosing (SUD) and treatment dose schedule de-escalation in the real-world (rw) setting – an analysis of multicenter electronic medical records
Abstract #P1940	Exploratory analysis to identify response-related biomarkers in the China cohort of the Phase 1/2 MajesTEC-1 trial of teclistamab for triple-class exposed RRMM
Abstract #P1960	Efficacy and safety of talquetamab, a GPRC5D×CD3 bispecific antibody, in Chinese patients with RRMM from the Phase 1/2 MonumenTAL-1 study
Abstract #1970	Indirect treatment comparisons of daratumumab-pomalidomide-dexamethasone (DPd) and pomalidomide-bortezomib-dexamethasone (PVd) in RRMM
Abstract #1973	Real-world observations on the evolving treatment landscape and improved survival outcomes for multiple myeloma patients in Finland
Abstract #P1981	Real-world treatment patterns, efficacy, and safety of daratumumab-based regimens in Chinese patients with multiple myeloma: an updated analysis of the MMY4032 study
Abstract #P1987	Epidemiology and real-world management of monoclonal gammopathies patients in Spain by based natural language and artificial intelligence, the CIMMA study
B-Cell Malignancies	
Poster Presentations	
Abstract #P632	CLL and SLL patient demographics and patient-reported burden in ibrutinib and non-ibrutinib receivers in the US: a real-world study
Abstract #P664	First-line (1L) ibrutinib in patients with CLL demonstrates OS comparable to an age-matched European population
Abstract #P670	Final analysis of the RESONATE-2 study: up to 10 years of follow-up of first-line ibrutinib treatment in patients with CLL/SLL
Abstract #P675	Outcomes in high-risk subgroups after fixed-duration ibrutinib plus venetoclax for CLL/SLL: up to 5.5 years of follow-up in the Phase 2 CAPTIVATE study
Abstract #P694	Comparative effectiveness of ibrutinib flexible dosing treatment strategies on time to next treatment in a largely community-based claims database: a target trial emulation study
Abstract #P696	Comparison of time to next treatment between patients with CLL initiating first-line ibrutinib or acalabrutinib overall and in a subgroup with high-risk characteristics
Abstract #P699	6-Year time to next treatment (TTNT) extrapolation curve for GLOW study: first-line ibrutinib plus venetoclax offers long treatment-free period for elderly/unfit CLL patients
Abstract #P704	IBROMICS: a real-world study of clinical and biological parameters determining response in patients with CLL treated in first line with single agent ibrutinib
Abstract #P1128	Efficacy and safety of ibrutinib plus venetoclax in patients with MCL and TP53 mutations in the SYMPATICO study
Abstract #P1835	Cross-study comparison of ibrutinib in combination with venetoclax versus venetoclax in combination with obinutuzumab in subjects with previously untreated CLL with comorbidities
Abstract #P1846	Real-world clinical outcomes of first-line ibrutinib dose reduction versus acalabrutinib among patients with CLL or SLL
Abstract #P2070	Dose adjustment outcomes in patients with Waldenström's macroglobulinemia treated with ibrutinib
Myeloid Malignancies	
Oral Presentations	

Abstract #S133	A Phase 1b study of the Menin-KMT2A Inhibitor JNJ-75276617 in combination with venetoclax and azacitidine in relapsed/refractory acute myeloid leukemia (AML) with alterations in KMT2A or NPM1
Poster Presentations	
Abstract #P1017	T-cell phenotyping supports the use of T-cell engaging antibodies for treatment of calreticulin mutated myeloproliferative neoplasms
Abstract #P1545	OS of patients with warm autoimmune hemolytic anemia in Sweden: a nationwide population-based study
Abstract #P1806	Treatment patterns and molecular testing across the patient journey: a real-world analysis in a US-based cohort of newly diagnosed and relapsed/refractory AML patients

About RYBREVANT®

RYBREVANT® (amivantamab-vmjw), a fully-human bispecific antibody targeting *EGFR* and MET with immune cell-directing activity, is approved in the **U.S.**, **Europe**, and in other markets around the world as monotherapy 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.[1]

RYBREVANT® is also approved in the U.S. in combination with chemotherapy (carboplatin and pemetrexed) for the first-line treatment of adult patients with locally advanced or metastatic NSCLC with *EGFR* exon 20 insertion mutations, as detected by an FDA-approved test. In October 2023, a type II extension of indication application was **submitted** to the European Medicines Agency (EMA) seeking approval of RYBREVANT® for this indication.

In December 2023, Johnson & Johnson **submitted** a supplemental Biologics License Application (sBLA) together with a New Drug Application (NDA) to the U.S. FDA for RYBREVANT® in combination with lazertinib for the first-line treatment of adult patients with locally advanced or metastatic NSCLC with *EGFR* exon 19 deletions or L858R substitution mutations, as detected by an FDA-approved test. This submission is based on the Phase 3 MARIPOSA study and was granted Priority Review in February 2024. A marketing authorization application (MAA) and type II extension of indication application were also submitted to the EMA seeking approval of lazertinib in combination with RYBREVANT® based on the MARIPOSA study.

In November 2023, Johnson & Johnson **submitted** an sBLA to the U.S. FDA for RYBREVANT® in combination with chemotherapy for the treatment of patients with *EGFR*-mutated NSCLC who progressed on or after osimertinib based on the MARIPOSA-2 study. A type II extension of indication application was also **submitted** to the EMA seeking approval of RYBREVANT® for this indication.

The NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for NSCLC§ prefer next-generation sequencing–based strategies over polymerase chain reaction–based approaches for the detection of *EGFR* exon 20 insertion variants. The NCCN Guidelines include:

- Amivantamab-vmjw (RYBREVANT®) plus carboplatin and pemetrexed as a preferred (Category 1 recommendation) first-line therapy in treatment-naive patients with newly diagnosed advanced or metastatic *EGFR* exon 20 insertion mutation-positive advanced NSCLC, or as a subsequent therapy option (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.[2] †‡

- Amivantamab-vmjw (RYBREVANT®) plus chemotherapy as a preferred (Category 1 recommendation) subsequent therapy for patients with locally advanced or metastatic NCSLC with *EGFR* exon 19 deletions or exon 21 L858R mutations who experienced disease progression after treatment with osimertinib.[2] †‡

- Amivantamab-vmjw (RYBREVANT®) as a subsequent therapy option (Category 2A recommendation) for patients that have progressed on or after platinum-based chemotherapy with or without an immunotherapy and have *EGFR* exon 20 insertion mutation-positive NSCLC.[2] †‡

RYBREVANT® is being studied in multiple clinical trials in NSCLC, including:

- The Phase 3 PAPILLON (NCT04538664) study assessing RYBREVANT® in combination with carboplatin-pemetrexed versus chemotherapy alone in the first-line treatment of patients with advanced or metastatic NSCLC with *EGFR* exon 20 insertion mutations. Topline data for this randomized Phase 3 study demonstrated statistically significant and clinically meaningful improvement in progression-free survival (PFS) in patients receiving RYBREVANT®.[3]

- The Phase 3 MARIPOSA-2 (NCT04988295) study assessing the efficacy of RYBREVANT® (with or without lazertinib) and carboplatin-pemetrexed versus carboplatin-pemetrexed alone in patients with locally advanced or metastatic *EGFR* ex19del or L858R substitution NSCLC after disease progression on or after osimertinib. Topline data for this randomized Phase 3 study demonstrated statistically significant and clinically meaningful improvement in PFS in these patients receiving RYBREVANT® plus chemotherapy with and without lazertinib versus chemotherapy.[4]

- The Phase 3 MARIPOSA (NCT04487080) study assessing RYBREVANT® in combination with lazertinib versus osimertinib and versus lazertinib alone in the first-line treatment of patients with locally advanced or metastatic NSCLC with *EGFR* ex19del or L858R substitution mutations. Topline data for this randomized Phase 3 study demonstrated statistically significant and clinically meaningful improvement in PFS in patients receiving RYBREVANT® plus lazertinib versus osimertinib.[5]

- The Phase 1 CHRYSALIS (NCT02609776) study evaluating RYBREVANT® in patients with advanced NSCLC.[6]

- The Phase 1/1b CHRYSALIS-2 (NCT04077463) study evaluating RYBREVANT® in combination with lazertinib and lazertinib as a monotherapy in patients with advanced NSCLC with *EGFR* mutations.[7]

- The Phase 1 PALOMA (NCT04606381) study assessing the feasibility of subcutaneous administration of amivantamab based on safety and pharmacokinetics and to determine a dose, dose regimen and formulation for amivantamab subcutaneous delivery.[8]

- The Phase 2 PALOMA-2 (NCT05498428) study assessing subcutaneous amivantamab in patients with advanced or metastatic solid tumors including *EGFR*-mutated NSCLC.[9]

- The Phase 3 PALOMA-3 (NCT05388669) study assessing lazertinib with subcutaneous amivantamab compared to intravenous amivantamab in patients with *EGFR*-mutated advanced or metastatic NSCLC.[10]

- The Phase 1/2 METalmark (NCT05488314) study assessing RYBREVANT® and capmatinib combination therapy in locally advanced or metastatic NSCLC.[11]

- The Phase 1/2 PolyDamas (NCT05908734) study assessing RYBREVANT® and cetrelimab combination therapy in locally advanced or metastatic NSCLC.[12]

- The Phase 2 SKIPPirr study (NCT05663866) exploring how to decrease the incidence and/or severity of first-dose infusion-related reactions with RYBREVANT® in combination with lazertinib in relapsed or refractory *EGFR*-mutated advanced or metastatic NSCLC.[13]

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

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 metastatic castration-sensitive prostate cancer (mCSPC).[14] ERLEADA® received U.S. Food and Administration (FDA) approval for nmCRPC in February 2018 and received U.S. FDA approval for mCSPC in September 2019. To date, more than 200,000 patients worldwide have been treated with ERLEADA®. Additional studies are ongoing in the evaluation of ERLEADA® for the treatment of localized high-risk or locally advanced prostate cancer including the Phase 3 ATLAS 15 (NCT02531516) and PROTEUS (NCT03767244) studies.

For more information, visit www.ERLEADA.com.

About BALVERSA®

BALVERSA® (erdafitinib) is a once-daily, oral *FGFR* kinase inhibitor indicated for the treatment of adult patients with locally advanced or mUC with susceptible fibroblast growth factor receptor 3 *(FGFR3*) genetic alterations whose disease has progressed on or after at least one line of prior systemic therapy. BALVERSA® is not recommended for the treatment of patients who are eligible for and have not received prior PD-1 or PD-(L)1 inhibitor therapy.[15] 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.

BALVERSA® received Breakthrough Therapy Designation from the U.S. FDA in 2018 and received full approval in 2024 for the treatment of adults with locally advanced or mUC that has susceptible *FGFR3* or fibroblast growth factor receptor 2 *(FGFR2)* genetic alterations and who have progressed during or following at least one line of prior platinum-containing chemotherapy, including within 12 months of neoadjuvant or adjuvant platinum-containing chemotherapy.[16] Full approval was based on the clinical and overall survival benefited in the Phase 3 THOR study.

The Company submitted a marketing authorization application to the European Medicines Agency in September 2023 for BALVERSA ® as a treatment for adult patients with *FGFR3-altered*, locally advanced unresectable or mUC that has progressed following therapy with a PD-L1 inhibitor.

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

For more information, visit www.BALVERSA.com.

About CARVYKTI® (ciltacabtagene autoleucel; cilta-cel)

CARVYKTI® (cilta-cel) received U.S. Food and Drug Administration approval 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.[17] CARVYKTI® is now approved in the U.S. for the treatment of adult patients with relapsed or refractory myeloma who have received at least one prior line of therapy including a proteasome inhibitor, an immunomodulatory agent, and who are refractory to lenalidomide. In addition to a unanimous (11 to 0) FDA Oncologic Drugs Advisory Committee (ODAC) recommendation in support of this new indication, in April 2024, the European Commission approved a Type II variation for CARVYKTI® for the treatment of adults with relapsed and refractory multiple myeloma who have received at least one prior therapy, including an immunomodulatory agent and a proteasome inhibitor, have demonstrated disease progression on the last therapy, and are refractory to lenalidomide. CARVYKTI® is a B-cell maturation antigen (BCMA)-directed, genetically modified autologous T-cell immunotherapy, which involves reprogramming a patient's own T-cells with a transgene encoding 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 domains 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., a Johnson & Johnson company, entered into an exclusive worldwide license and collaboration agreement with Legend Biotech USA, Inc. to develop and commercialize CARVYKTI®.

For more information, visit www.CARVYKTI.com.

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.[18] 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.[19]

DARZALEX® is the first CD38-directed antibody approved to treat multiple myeloma.[20] DARZALEX®-based regimens have been used in the treatment of more than 518,000 patients worldwide and more than 68,000 patients in the U.S. alone.

In August 2012, Janssen Biotech, Inc., a Johnson & Johnson company, 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, the NCCN® guidelines recommend daratumumab in combination with lenalidomide and dexamethasone as a Category 1 preferred regimen in non-transplant candidates; daratumumab in combination with bortezomib, melphalan, and prednisone as another recommended Category 1 regimen for non-transplant candidates; and daratumumab in combination with bortezomib, thalidomide and dexamethasone as a Category 2A regimen useful in certain circumstances for transplant candidates. 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.

About TECVAYLI®

TECVAYLI® (teclistamab-cqyv) received approval from the U.S. FDA in October 2022 as an off-the-shelf (or ready-to-use) antibody that is administered as a subcutaneous treatment for adult patients with relapsed or refractory multiple myeloma (RRMM) who have received at least four prior lines of therapy, including a proteasome inhibitor, an immunomodulatory agent and an anti-CD38 antibody.[2] The European Commission (EC) granted TECVAYLI® conditional marketing authorization (CMA) in August 2022 as monotherapy for the treatment of adult patients with RRMM who have received at least three prior therapies, including a proteasome inhibitor, an immunomodulatory agent and an anti-CD38 antibody, and have demonstrated disease progression since the last therapy. In August 2023, the EC granted the approval of a Type II variation application for TECVAYLI®, providing the option for a reduced dosing frequency of 1.5 mg/kg every two weeks in patients who have achieved a complete response (CR) or better for a minimum of six months. TECVAYLI® is a first-in-class, bispecific T-cell engager antibody therapy that uses innovative science to activate the immune system by binding to the CD3 receptor expressed on the surface of T-cells and to the B-cell maturation antigen (BCMA) expressed on the surface of multiple myeloma cells and some healthy B-lineage cells. In February 2024, the U.S. FDA approved the supplemental Biologics License Application (sBLA) for TECVAYLI® for a reduced dosing frequency of 1.5 mg/kg every two weeks (Q2W) in patients with relapsed or refractory multiple myeloma who have achieved and maintained a CR or better for a minimum of six months.
For more information, visit www.TECVAYLI.com.

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 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 inhibit their proliferation.[21, 22, 23]

IMBRUVICA® is approved in more than 100 countries and has been used to treat almost 300,000 patients worldwide over the last decade. There are more than 50 company-sponsored clinical trials, including 18 Phase 3 studies, spanning more than 11 years evaluating the efficacy and safety of IMBRUVICA®.

IMBRUVICA® was first approved by the U.S. FDA in November 2013, and today is indicated for adult patients in four disease areas. These include indications to treat adults with chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma (SLL) with or without 17p deletion (del17p); adults with Waldenström's macroglobulinemia (WM); and adult and pediatric patients aged one year and older with previously treated chronic graft versus host disease (cGVHD) after failure of one or more lines of systemic therapy.[24]

About TALVEY®

TALVEY® (talquetamab-tgvs) received approval from the U.S. FDA in August 2023 as a first-in-class bispecific antibody for the treatment of adult patients with relapsed or refractory multiple myeloma who have received at least four prior lines of therapy, including a proteasome inhibitor, an immunomodulatory agent, and an anti-CD38 antibody.[25] The European Commission (EC) has granted conditional marketing authorization (CMA) of TALVEY® (talquetamab) in August 2023 as monotherapy for the treatment of adult patients with relapsed and refractory multiple myeloma (RRMM) who have received at least three prior therapies, including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 antibody, and have demonstrated disease progression on the last therapy.[26]

TALVEY® is a bispecific T-cell engaging antibody that binds to the CD3 receptor expressed on the surface of T cells and G protein-coupled receptor class C group 5 member D (GPRC5D), a novel multiple myeloma target which is highly expressed on the surface of multiple myeloma cells and non-malignant plasma cells, as well as some healthy tissues such as epithelial cells of the skin and tongue.

For more information, visit www.TALVEY.com.

About nipocalimab

Nipocalimab is an investigational, high-affinity, fully human, aglycosylated, effectorless, monoclonal antibody that aims to selectively block fragment crystallizable receptor (FcRn) to reduce levels of circulating immunoglobulin G (IgG antibodies, including autoantibodies and alloantibodies that underlie multiple conditions.[27] Nipocalimab is the only FcRn blocker being studied across three key segments in the autoantibody space: Rare Autoantibody diseases (e.g., generalized myasthenia gravis in adults and children, chronic inflammatory demyelinating polyneuropathy, warm autoimmune hemolytic anemia, and idiopathic inflammatory myopathies); Maternal Fetal diseases mediated by maternal alloantibodies (e.g., hemolytic disease of the fetus and newborn and fetal and neonatal alloimmune thrombocytopenia); and Prevalent Rheumatology (e.g., rheumatoid arthritis, Sjögren's disease, and systemic lupus erythematosus).[28,29,30,31,32,33,34,35,36] Blockade of FcRn has the potential to reduce overall IgG including pathogenic alloantibody levels while preserving immune function without causing broad immunosuppression. Blockade of IgG binding to FcRn in the placenta is also believed to prevent transplacental transfer of maternal alloantibodies to the fetus.[37,38]

RYBREVANT® IMPORTANT SAFETY INFORMATION

INDICATIONS AND USAGE

RYBREVANT® is a bispecific EGF receptor-directed and MET receptor-directed antibody indicated:

- in combination with carboplatin and pemetrexed for the first-line treatment of adult patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) with epidermal growth factor receptor (*EGFR*) exon 20 insertion mutations, as detected by an FDA-approved test.
- as a single agent 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.

WARNINGS AND PRECAUTIONS

The safety population of RYBREVANT® with carboplatin and pemetrexed described in Warnings and Precautions was based on 151 patients in the PAPILLON study.

The safety population of RYBREVANT® as a single agent described in Warnings and Precautions was based on 129 patients in the CHRYSALIS study.

Infusion-Related Reactions

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

RYBREVANT® with Carboplatin and Pemetrexed

RYBREVANT® in combination with carboplatin and pemetrexed can cause infusion-related reactions. Based on the safety population, infusion-related reactions occurred in 42% of patients treated with RYBREVANT® in combination with carboplatin and pemetrexed, including Grade 3 (1.3%) adverse reactions. The incidence of infusion modifications due to IRR was 40%, and 0.7% of patients permanently discontinued RYBREVANT®.

RYBREVANT® as a Single Agent

Based on the safety population, IRR occurred in 66% of patients treated with RYBREVANT® as a single agent. 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/Pneumonitis

RYBREVANT® can cause interstitial lung disease (ILD)/pneumonitis.

RYBREVANT® with Carboplatin and Pemetrexed

Based on the safety population, Grade 3 ILD/pneumonitis occurred in 2.6% of patients treated with RYBREVANT in combination with carboplatin and pemetrexed, all patients required permanent discontinuation.

RYBREVANT® as a Single Agent

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 Reactions

RYBREVANT® can cause rash (including dermatitis acneiform), pruritus and dry skin.

RYBREVANT® with Carboplatin and Pemetrexed

RYBREVANT® in combination with carboplatin and pemetrexed can cause dermatologic adverse reactions. Based on the safety population, rash occurred in 89% of patients treated with RYBREVANT® in combination with carboplatin and pemetrexed, including Grade 3 (19%) adverse reactions. Rash leading to dose reductions occurred in 19% of patients, and 2% permanently discontinued RYBREVANT® and 1.3% discontinued pemetrexed.

RYBREVANT® as a Single Agent

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® as a single agent.

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 Toxicity

RYBREVANT® can cause ocular toxicity including keratitis, dry eye symptoms, conjunctival redness, blurred vision, visual impairment, ocular itching, and uveitis.

RYBREVANT® with Carboplatin and Pemetrexed

Based on the safety population RYBREVANT® in combination with carboplatin and pemetrexed can cause ocular toxicity including blepharitis, dry eye, conjunctival redness, blurred vision, and eye pruritus. All events were Grade 1-2.

RYBREVANT® as a Single Agent

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 Toxicity

Based on its mechanism of action and findings from animal models, RYBREVANT® can cause fetal harm when administered to a pregnant woman. Administration of other *EGFR* inhibitor molecules to pregnant animals has resulted in an increased incidence of impairment of embryo-fetal development, embryo lethality, and abortion. 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 last dose of RYBREVANT®.

Adverse Reactions

RYBREVANT® with Carboplatin and Pemetrexed

For the 151 patients in the PAPILLON clinical trial who received RYBREVANT® in combination with carboplatin and pemetrexed the most common adverse reactions (≥ 20%) were rash (90%), nail toxicity (62%), stomatitis (43%), infusion-related reaction (42%), fatigue (42%), edema (40%), constipation (40%), decreased appetite (36%), nausea (36%), COVID-19 (24%), diarrhea (21%), and vomiting (21%). The most common Grade 3 to 4 laboratory abnormalities (≥ 2%) were decreased albumin (7%), increased alanine aminotransferase (4%), increased gamma-glutamyl transferase (4%), decreased sodium (7%), decreased potassium (11%), decreased magnesium (2%), and decreases in white blood cells (17%), hemoglobin (11%), neutrophils (36%), platelets (10%), and lymphocytes (11%).

Serious adverse reactions occurred in 37% of patients who received RYBREVANT® in combination with carboplatin and pemetrexed. Serious adverse reactions in ≥ 2% of patients included rash, pneumonia, ILD, pulmonary embolism, vomiting and COVID-19. Fatal adverse reactions occurred in 7 patients (4.6%) due to pneumonia, cerebrovascular accident, cardio-respiratory arrest, COVID-19, sepsis, and death not otherwise specified.

RYBREVANT® as a Single Agent

For the 129 patients in the CHRYSALIS clinical trial who received RYBREVANT® as a single agent the most common adverse reactions (≥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 (≥2%) were decreased lymphocytes (8%), decreased albumin (8%), decreased phosphate (8%), decreased potassium (6%), increased alkaline phosphatase (4.8%), increased glucose (4%), increased gamma-gutamyl transferase (4%), and decreased sodium (4%).

Serious adverse reactions occurred in 30% of patients who received RYBREVANT®. Serious adverse reactions in ≥ 2% of patients included pulmonary embolism, pneumonitis/ILD, dyspnea, musculoskeletal pain, pneumonia, and muscular weakness. Fatal adverse reactions occurred in 2 patients (1.5%) due to pneumonia and 1 patient (0.8%) due to sudden death.

Please read the full Prescribing Information for RYBREVANT®.

ERLEADA® IMPORTANT SAFETY INFORMATION

INDICATIONS

ERLEADA is an androgen receptor inhibitor indicated for the treatment of patients with:

- metastatic castration-sensitive prostate cancer (mCSPC)
- non-metastatic castration-resistant prostate cancer (nmCRPC)

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.

Severe Cutaneous Adverse Reactions — Fatal and life-threatening cases of severe cutaneous adverse reactions (SCARs), including Stevens-Johnson syndrome/toxic epidermal necrolysis (SJS/TEN), and drug reaction with eosinophilia and systemic symptoms (DRESS) occurred in patients receiving ERLEADA®.

Monitor patients for the development of SCARs. Advise patients of the signs and symptoms of SCARs (eg, a prodrome of fever, flu-like symptoms, mucosal lesions, progressive skin rash, or lymphadenopathy). If a SCAR is suspected, interrupt ERLEADA® until the etiology of the reaction has been determined. Consultation with a dermatologist is recommended. If a SCAR is confirmed, or for other Grade 4 skin reactions, permanently discontinue ERLEADA® *[see Dosage and Administration (2.2)].*

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 (≥10%) that occurred more frequently in the ERLEADA®-treated patients (≥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®.

BALVERSA® IMPORTANT SAFETY INFORMATION

INDICATIONS AND USAGE

BALVERSA is a kinase inhibitor indicated for the treatment of adult patients with locally advanced or metastatic urothelial carcinoma (mUC) with susceptible *FGFR3* genetic alterations whose disease has progressed on or after at least one line of prior systemic therapy.

Select patients for therapy based on an FDA-approved companion diagnostic for BALVERSA®.

Limitations of Use

BALVERSA is not recommended for the treatment of patients who are eligible for and have not received prior PD-1 or PD-L1 inhibitor therapy. Information on FDA-approved tests for the detection of FGFR3 genetic alterations in urothelial cancer is available at: https://www.fda.gov/CompanionDiagnostics.

WARNING AND PRECAUTIONS

The safety population described in the Warnings and Precautions reflect a pooled safety population of 479 patients with advanced urothelial cancer and *FGFR* alterations who received BALVERSA®.

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

CSR/RPED occurred in 22% of patients treated with BALVERSA®, with a median time to first onset of 46 days. In 104 patients with CSR, 40% required dose interruptions and 56% required dose reductions; 2.9% of BALVERSA®-treated patients required permanent discontinuation for CSR. Of the 24 patients who restarted BALVERSA® after dose interruption with or without dose reduction, 67% had recurrence and/or worsening of CSR after restarting. CSR was ongoing in 41% of the 104 patients at the time of last evaluation.

Dry eye symptoms occurred in 26% of BALVERSA®-treated 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, fundoscopy, and optical coherence tomography. Withhold or permanently discontinue BALVERSA® based on severity and/or ophthalmology exam findings.

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®. Increased phosphate occurred in 73% of BALVERSA®-treated patients. The median onset time of increased phosphate was 16 days (range: 8–421) after initiating BALVERSA®. Twenty-four percent of patients received phosphate binders during treatment with BALVERSA®. Vascular calcification was observed in 0.2% of patients treated with BALVERSA®.

Monitor for hyperphosphatemia throughout treatment. In all patients, restrict phosphate intake to 600-800 mg daily and avoid concomitant use of agents that may increase serum phosphate levels. If serum phosphate is above 7.0 mg/dL, consider adding an oral phosphate binder until serum phosphate level returns to <7.0 mg/dL. Withhold, dose reduce, or permanently discontinue BALVERSA® based on duration and severity of hyperphosphatemia.

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 female. In a rat embryo-fetal toxicity study, erdafitinib caused malformations and embryo-fetal death at maternal exposures that were less than the human exposures at the maximum human recommended dose based on AUC. Advise pregnant patients 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.

Adverse Reactions

In this pooled safety population described in Warnings and Precautions, the median duration of treatment was 4.8 months (range: 0.1 to 43 months). The most common (>20%) adverse reactions, including laboratory abnormalities, were increased phosphate, nail disorders, stomatitis, diarrhea, increased creatinine, increased alkaline phosphatase, increased alanine aminotransferase, decreased hemoglobin, decreased sodium, increased aspartate aminotransferase, fatigue, dry mouth, dry skin, decreased phosphate, decreased appetite, dysgeusia, constipation, increased calcium, dry eye, palmar-plantar erythrodysesthesia syndrome, increased potassium, alopecia, and central serous retinopathy.

In Cohort 1 of the BLC3001 (NCT03390504, THOR) study:

- Serious adverse reactions occurred in 41% of patients who received BALVERSA®. Serious reactions in >2% of patients included urinary tract infection (4.4%), hematuria (3.7%), hyponatremia (2.2%), and acute kidney injury (2.2%). Fatal adverse reactions occurred in 4.4% of patients who received BALVERSA®, including sudden death (1.5%), pneumonia (1.5%), renal failure (0.7%), and cardiorespiratory arrest (0.7%).

- Permanent discontinuation of BALVERSA® due to an adverse reaction occurred in 14% of patients. Adverse reactions which resulted in permanent discontinuation of BALVERSA® in >2% of patients included nail disorders (3%) and eye disorders (2.2%).

- Dosage interruptions of BALVERSA® due to an adverse reaction occurred in 72% of patients. Adverse reactions which required dosage interruption in >4% of patients included nail disorders (22%), stomatitis (19%), eye disorders (16%), palmar-plantar erythrodysesthesia syndrome (15%), diarrhea (10%), hyperphosphatemia (7%), increased aspartate aminotransferase (6%), and increased alanine aminotransferase (5%).

- Dose reductions of BALVERSA® due to an adverse reaction occurred in 69% of patients. Adverse reactions which required dose reductions in >4% of patients included nail disorders (27%), stomatitis (19%), eye disorders (17%), palmar-plantar erythrodysesthesia syndrome (12%), diarrhea (7%), dry mouth (4.4%), and hyperphosphatemia (4.4%).

- Clinically relevant adverse reactions in <15% of patients who received BALVERSA® included nausea (15%), pyrexia (15%), epistaxis (13%), vomiting (10%), and arthralgia (10%).

Drug Interactions

Effects of Other Drugs on BALVERSA®

- Moderate CYP2C9 or Strong CYP3A4 Inhibitors: Consider alternative agents; however, if co-administration is unavoidable, monitor closely for adverse reactions.

- Strong CYP3A4 inducers: Avoid co-administration with BALVERSA®.

- Moderate CYP3A4 inducers: If co-administration is required at the start of BALVERSA® treatment, administer BALVERSA® at a dose of 9 mg daily.

- Serum phosphate level-altering agents: Avoid co-administration with agents that can alter serum phosphate levels before the initial dose increase period based on serum phosphate levels.

Effect of BALVERSA® on Other Drugs

- P-gp substrates: If co-administration is unavoidable, separate BALVERSA® administration by at least 6 hours before or after administration of P-gp substrates with narrow therapeutic indices.

Please click here to see full BALVERSA® Prescribing Information.

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, who have received at least 1 prior line of therapy, including a proteasome inhibitor and an immunomodulatory agent, and are refractory to lenalidomide.

IMPORTANT SAFETY INFORMATION

WARNING: CYTOKINE RELEASE SYNDROME, NEUROLOGIC TOXICITIES, HLH/MAS, PROLONGED and RECURRENT CYTOPENIA, and SECONDARY HEMATOLOGICAL MALIGNANCIESCytokine 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 (GBS) 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®. Secondary hematological malignancies, including myelodysplastic syndrome and acute myeloid leukemia, have occurred in patients following treatment with CARVYKTI®. T-cell malignancies have occurred following treatment of hematologic malignancies with BCMA- and CD19-directed genetically modified autologous T-cell immunotherapies, including 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

Increased early mortality - In CARTITUDE-4, a (1:1) randomized controlled trial, there was a numerically higher percentage of early deaths in patients randomized to the CARVYKTI® treatment arm compared to the control arm. Among patients with deaths occurring within the first 10 months from randomization, a greater proportion (29/208; 14%) occurred in the CARVYKTI® arm compared to (25/211; 12%) in the control arm. Of the 29 deaths that occurred in the CARVYKTI® arm within the first 10 months of randomization, 10 deaths occurred prior to CARVYKTI® infusion, and 19 deaths occurred after CARVYKTI® infusion. Of the 10 deaths that occurred prior to CARVYKTI® infusion, all occurred due to disease progression, and none occurred due to adverse events. Of the 19 deaths that occurred after CARVYKTI® infusion, 3 occurred due to disease progression, and 16 occurred due to adverse events. The most common adverse events were due to infection (n=12).

Cytokine release syndrome (CRS), including fatal or life-threatening reactions, occurred following treatment with CARVYKTI®. Among patients receiving CARVYKTI® for RRMM in the CARTITUDE-1 & 4 studies (N=285), CRS occurred in 84% (238/285), including ≥Grade 3 CRS (ASCT 2019) in 4% (11/285) of patients. Median time to onset of CRS, any grade, was 7 days (range: 1 to 23 days). CRS resolved in 82% with a median duration of 4 days (range: 1 to 97 days). The most common manifestations of CRS in all patients combined (≥10%) included fever (84%), hypotension (29%) and aspartate aminotransferase increased (11%). Serious events that may be associated with CRS include pyrexia, hemophagocytic lymphohistiocytosis, respiratory failure, disseminated intravascular coagulation, capillary leak syndrome, and supraventricular and ventricular tachycardia. CRS occurred in 78% of patients in CARTITUDE-4 (3% Grade 3 to 4) and in 95% of patients in CARTITUDE-1 (4% Grade 3 to 4).

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.

Ensure that a minimum of two doses of tocilizumab are available prior to infusion of CARVYKTI®.

Of the 285 patients who received CARVYKTI® in clinical trials, 53% (150/285) patients received tocilizumab; 35% (100/285) received a single dose, while 18% (50/285) received more than 1 dose of tocilizumab. Overall, 14% (39/285) of patients received at least one dose of corticosteroids for treatment of CRS.

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, GBS, immune mediated myelitis, 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.

Among patients receiving CARVYKTI® in the CARTITUDE-1 & 4 studies for RRMM, one or more neurologic toxicities occurred in 24% (69/285), including ≥Grade 3 cases in 7% (19/285) of patients. Median time to onset was 10 days (range: 1 to 101) with 63/69 (91%) of cases developing by 30 days. Neurologic toxicities resolved in 72% (50/69) of patients with a median duration to resolution of 23 days (range: 1 to 544). Of patients developing neurotoxicity, 96% (66/69) also developed CRS. Subtypes of neurologic toxicities included ICANS in 13%, peripheral neuropathy in 7%, cranial nerve palsy in 7%, parkinsonism in 3%, and immune mediated myelitis in 0.4% of the patients.

Immune Effector Cell-associated Neurotoxicity Syndrome (ICANS): Patients receiving CARVYKTI® 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.

Among patients receiving CARVYKTI® in the CARTITUDE-1 & 4 studies, ICANS occurred in 13% (36/285), including Grade ≥3 in 2% (6/285) of the patients. Median time to onset of ICANS was 8 days (range: 1 to 28 days). ICANS resolved in 30 of 36 (83%) of patients with a median time to resolution of 3 days (range: 1 to 143 days). Median duration of ICANS was 6 days (range: 1 to 1229 days) in all patients including those with ongoing neurologic events at the time of death or data cut off. Of patients with ICANS 97% (35/36) had CRS. The onset of ICANS occurred during CRS in 69% of patients, before and after the onset of CRS in 14% of patients respectively.

Immune Effector Cell-associated Neurotoxicity Syndrome occurred in 7% of patients in CARTITUDE-4 (0.5% Grade 3) and in 23% of patients in CARTITUDE-1 (3% Grade 3). The most frequent ≥2% manifestations of ICANS included encephalopathy (12%), aphasia (4%), headache (3%), motor dysfunction (3%), ataxia (2%) and sleep disorder (2%).

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: Neurologic toxicity with parkinsonism has been reported in clinical trials of CARVYKTI®. Among patients receiving CARVYKTI® in the CARTITUDE-1 & 4 studies, parkinsonism occurred in 3% (8/285), including Grade ≥ 3 in 2% (5/285) of the patients. Median time to onset of parkinsonism was 56 days (range: 14 to 914 days). Parkinsonism resolved in 1 of 8 (13%) of patients with a median time to resolution of 523 days. Median duration of parkinsonism was 243.5 days (range: 62 to 720 days) in all patients including those with ongoing neurologic events at the time of death or data cut off. The onset of parkinsonism occurred after CRS for all patients and after ICANS for 6 patients.

Parkinsonism occurred in 1% of patients in CARTITUDE-4 (no Grade 3 to 4) and in 6% of patients in CARTITUDE-1 (4% Grade 3 to 4).

Manifestations of parkinsonism included movement disorders, cognitive impairment, and personality changes. 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 GBS occurred following treatment with CARVYKTI® 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.

Immune mediated myelitis: Grade 3 myelitis occurred 25 days following treatment with CARVYKTI® in CARTITUDE-4 in a patient who received CARVYKTI® as subsequent therapy. Symptoms reported included hypoesthesia of the lower extremities and the lower abdomen with impaired sphincter control. Symptoms improved with the use of corticosteroids and intravenous immune globulin. Myelitis was ongoing at the time of death from other cause.

Peripheral neuropathy occurred following treatment with CARVYKTI®. Among patients receiving CARVYKTI® in the CARTITUDE-1 & 4 studies, peripheral neuropathy occurred in 7% (21/285), including Grade ≥3 in 1% (3/285) of the patients. Median time to onset of peripheral neuropathy was 57 days (range: 1 to 914 days). Peripheral neuropathy resolved in 11 of 21 (52%) of patients with a median time to resolution of 58 days (range: 1 to 215 days). Median duration of peripheral neuropathy was 149.5 days (range: 1 to 692 days) in all patients including those with ongoing neurologic events at the time of death or data cut off.

Peripheral neuropathies occurred in 7% of patients in CARTITUDE-4 (0.5% Grade 3 to 4) and in 7% of patients in CARTITUDE-1 (2% Grade 3 to 4). Monitor patients for signs and symptoms of peripheral neuropathies. Patients who experience peripheral neuropathy may also experience cranial nerve palsies or GBS.

Cranial nerve palsies occurred following treatment with CARVYKTI®. Among patients receiving CARVYKTI® in the CARTITUDE-1 & 4 studies, cranial nerve palsies occurred in 7% (19/285), including Grade ≥3 in 1% (1/285) of the patients. Median time to onset of cranial nerve palsies was 21 days (range: 17 to 101 days). Cranial nerve palsies resolved in 17 of 19 (89%) of patients with a median time to resolution of 66 days (range: 1 to 209 days). Median duration of cranial nerve palsies was 70 days (range: 1 to 262 days) in all patients including those with ongoing neurologic events at the time of death or data cut off. Cranial nerve palsies occurred in 9% of patients in CARTITUDE-4 (1% Grade 3 to 4) and in 3% of patients in CARTITUDE-1 (1% Grade 3 to 4).

The most frequent cranial nerve affected was the 7th cranial nerve. Additionally, cranial nerves III, V, and VI have been reported to be affected.

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): Among patients receiving CARVYKTI® in the CARTITUDE-1 & 4 studies, HLH/MAS occurred in 1% (3/285) of patients. All events of HLH/MAS had onset within 99 days of receiving CARVYKTI®, with a median onset of 10 days (range: 8 to 99 days) and all occurred in the setting of ongoing or worsening CRS. The manifestations of HLH/MAS included hyperferritinemia, hypotension, hypoxia with diffuse alveolar damage, coagulopathy and hemorrhage, cytopenia and multi-organ dysfunction, including renal dysfunction and respiratory failure.

Patients who develop HLH/MAS have an increased risk of severe bleeding. Monitor hematologic parameters in patients with HLH/MAS and transfuse per institutional guidelines. Fatal cases of HLH/MAS occurred following treatment with CARVYKTI®.

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 https://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.

Among patients receiving CARVYKTI® in the CARTITUDE-1 & 4 studies, Grade 3 or higher cytopenias not resolved by day 30 following CARVYKTI® infusion occurred in 62% (176/285) of the patients and included thrombocytopenia 33% (94/285), neutropenia 27% (76/285), lymphopenia 24% (67/285) and anemia 2% (6/285). After Day 60 following CARVYKTI® infusion 22%, 20%, 5%, and 6% of patients had a recurrence of Grade 3 or 4 lymphopenia, neutropenia, thrombocytopenia, and anemia respectively, after initial recovery of their Grade 3 or 4 cytopenia. Seventy-seven percent (219/285) 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. Sixteen and 25 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.

Among patients receiving CARVYKTI® in the CARTITUDE-1 & 4 studies, infections occurred in 57% (163/285), including ≥Grade 3 in 24% (69/285) of patients. Grade 3 or 4 infections with an unspecified pathogen occurred in 12%, viral infections in 6%, bacterial infections in 5%, and fungal infections in 1% of patients. Overall, 5% (13/285) of patients had Grade 5 infections, 2.5% of which were due to COVID-19. Patients treated with CARVYKTI® had an increased rate of fatal COVID-19 infections compared to the standard therapy arm.

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 5% of patients after CARVYKTI® 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. Counsel patients on the importance of prevention measures. Follow institutional guidelines for the vaccination and management of immunocompromised patients with COVID-19.

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: can occur in patients receiving treatment with CARVYKTI®. Among patients receiving CARVYKTI® in the CARTITUDE-1 & 4 studies, hypogammaglobulinemia adverse event was reported in 36% (102/285) of patients; laboratory IgG levels fell below 500mg/dl after infusion in 93% (265/285) of patients. Hypogammaglobulinemia either as an adverse reaction or laboratory IgG level below 500mg/dl, after infusion occurred in 94% (267/285) of patients treated. Fifty six percent (161/285) of patients received intravenous immunoglobulin (IVIG) post CARVYKTI® for either an adverse reaction or prophylaxis.

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 occurred following treatment with CARVYKTI®. Among patients receiving CARVYKTI® in the CARTITUDE-1 & 4 studies, hypersensitivity reactions occurred in 5% (13/285), all of which were ≤Grade 2. Manifestations of hypersensitivity reactions included flushing, chest discomfort, tachycardia, wheezing, tremor, burning sensation, non-cardiac chest pain, and pyrexia.

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 patients appropriately according to the severity of the hypersensitivity reaction.

Secondary Malignancies: Patients treated with CARVYKTI® may develop secondary malignancies. Among patients receiving CARVYKTI® in the CARTITUDE-1 & 4 studies, myeloid neoplasms occurred in 5% (13/285) of patients (9 cases of myelodysplastic syndrome, 3 cases of acute myeloid leukemia, and 1 case of myelodysplastic syndrome followed by acute myeloid leukemia). The median time to onset of myeloid neoplasms was 447 days (range: 56 to 870 days) after treatment with CARVYKTI®. Ten of these 13 patients died following the development of myeloid neoplasms; 2 of the 13 cases of myeloid neoplasm occurred after initiation of subsequent antimyeloma therapy. Cases of myelodysplastic syndrome and acute myeloid leukemia have also been reported in the post marketing setting. T-cell malignancies have occurred following treatment of hematologic malignancies with BCMA- and CD19-

directed genetically modified autologous T-cell immunotherapies, including CARVYKTI®. Mature T-cell malignancies, including CAR-positive tumors, may present as soon as weeks following infusions, and may include fatal outcomes.

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.

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 receiving CARVYKTI® 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 nonlaboratory adverse reactions (incidence greater than 20%) are pyrexia, cytokine release syndrome, hypogammaglobulinemia, hypotension, musculoskeletal pain, fatigue, infections-pathogen unspecified, 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 Grade 3 or 4 laboratory adverse reactions (incidence greater tha

or equal to 50%) include lymphopenia, neutropenia, white blood cell decreased, thrombocytopenia, and anemia.

Please read full Prescribing Information, including Boxed Warning, for CARVYKTI®.

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.

DARZALEX® 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
- 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® is contraindicated in patients with a history of severe hypersensitivity (eg, anaphylactic reactions) to daratumumab or any of the components of the formulation.

WARNINGS AND PRECAUTIONS

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, ie, 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®.

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 infusion. 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 is not impacted. Notify blood transfusion centers of this interference with serological testing and inform blood banks that a patient has received DARZALEX®. Type and screen patients prior to starting DARZALEX®.

Neutropenia and Thrombocytopenia

DARZALEX® 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® until recovery of neutrophils or for recovery of platelets.

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.

Embryo-Fetal Toxicity

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

The combination of DARZALEX® 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.

ADVERSE REACTIONS

The most frequently reported adverse reactions (incidence ≥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 (≥40%) with DARZALEX® are: neutropenia, lymphopenia, thrombocytopenia, leukopenia, and anemia.

Please click here to see the full Prescribing Information.

TECVAYLI® IMPORTANT SAFETY INFORMATION

WARNING: CYTOKINE RELEASE SYNDROME and NEUROLOGIC TOXICITY including IMMUNE EFFECTOR CELL-ASSOCIATED NEUROTOXICITY SYNDROME

- **Cytokine release syndrome (CRS), including life-threatening or fatal reactions, can occur in patients receiving TECVAYLI®. Initiate treatment with TECVAYLI® step-up dosing schedule to reduce risk of CRS. Withhold TECVAYLI® until CRS resolves or permanently discontinue based on severity.**
- **Neurologic toxicity, including Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS) and serious and life-threatening reactions, can occur in patients receiving TECVAYLI®. Monitor patients for signs or symptoms of neurologic toxicity, including ICANS, during treatment. Withhold TECVAYLI® until neurologic toxicity resolves or permanently discontinue based on severity.**
- **TECVAYLI® is available only through a restricted program called the TECVAYLI® and TALVEY® Risk Evaluation and Mitigation Strategy (REMS).**

INDICATION AND USAGE

TECVAYLI® (teclistamab-cqyv) is a bispecific B-cell maturation antigen (BCMA)-directed CD3 T-cell engager indicated for the treatment of adult patients with relapsed or refractory multiple myeloma who have received at least four prior lines of therapy, including a proteasome inhibitor, an immunomodulatory agent and an anti-CD38 monoclonal antibody.

This indication is approved under accelerated approval based on response rate. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trial(s).

WARNINGS AND PRECAUTIONS

Cytokine Release Syndrome - TECVAYLI® can cause cytokine release syndrome (CRS), including life-threatening or fatal reactions. In the clinical trial, CRS occurred in 72% of patients who received TECVAYLI® at the recommended dose, with Grade 1 CRS occurring in 50% of patients, Grade 2 in 21%, and Grade 3 in 0.6%. Recurrent CRS occurred in 33% of patients. Most patients experienced CRS following step-up dose 1 (42%), step-up dose 2 (35%), or the initial treatment dose (24%). Less than 3% of patients developed first occurrence of CRS following subsequent doses of TECVAYLI®. The median time to onset of CRS was 2 (range: 1 to 6) days after the most recent dose with a median duration of 2 (range: 1 to 9) days. Clinical signs and symptoms of CRS included, but were not limited to, fever, hypoxia, chills, hypotension, sinus tachycardia, headache, and elevated liver enzymes (aspartate aminotransferase and alanine aminotransferase elevation).

Initiate therapy according to TECVAYLI® step-up dosing schedule to reduce risk of CRS. Administer pretreatment medications to reduce risk of CRS and monitor patients following administration of TECVAYLI® accordingly. At the first sign of CRS, immediately evaluate patient for hospitalization. Administer supportive care based on severity and consider further management per current practice guidelines. Withhold or permanently discontinue TECVAYLI® based on severity.

TECVAYLI® is available only through a restricted program under a REMS.

Neurologic Toxicity including ICANS - TECVAYLI® can cause serious or life-threatening neurologic toxicity, including Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS).

In the clinical trial, neurologic toxicity occurred in 57% of patients who received TECVAYLI® at the recommended dose, with Grade 3 or 4 neurologic toxicity occurring in 2.4% of patients. The most frequent neurologic toxicities were headache (25%), motor dysfunction (16%), sensory neuropathy (15%), and encephalopathy (13%). With longer follow-up, Grade 4 seizure and fatal Guillain-Barré syndrome (one patient each) occurred in patients who received TECVAYLI®.

In the clinical trial, ICANS was reported in 6% of patients who received TECVAYLI® at the recommended dose. Recurrent ICANS occurred in 1.8% of patients. Most patients experienced ICANS following step-up dose 1 (1.2%), step-up dose 2 (0.6%), or the initial treatment dose (1.8%). Less than 3% of patients developed first occurrence of ICANS following subsequent doses of TECVAYLI®. The median time to onset of ICANS was 4 (range: 2 to 8) days after the most recent dose with a median duration of 3 (range: 1 to 20) days. The most frequent clinical manifestations of ICANS reported were confusional state and dysgraphia. The onset of ICANS can be concurrent with CRS, following resolution of CRS, or in the absence of CRS.

Monitor patients for signs and symptoms of neurologic toxicity during treatment. At the first sign of neurologic toxicity, including ICANS, immediately evaluate patient and provide supportive therapy based on severity. Withhold or permanently discontinue TECVAYLI® based on severity per recommendations and consider further management per current practice guidelines.

Due to the potential for neurologic toxicity, patients are at risk of depressed level of consciousness. Advise patients to refrain from driving or operating heavy or potentially dangerous machinery during and for 48 hours after completion of TECVAYLI® step-up dosing schedule and in the event of new onset of any neurologic toxicity symptoms until neurologic toxicity resolves.

TECVAYLI® is available only through a restricted program under a REMS.

TECVAYLI® and TALVEY® REMS - TECVAYLI® is available only through a restricted program under a REMS called the TECVAYLI® and TALVEY® REMS because of the risks of CRS and neurologic toxicity, including ICANS.

Hepatotoxicity - TECVAYLI® can cause hepatotoxicity, including fatalities. In patients who received TECVAYLI® at the recommended dose in the clinical trial, there was one fatal case of hepatic failure. Elevated aspartate aminotransferase (AST) occurred in 34% of patients, with Grade 3 or 4 elevations in 1.2%. Elevated alanine aminotransferase (ALT) occurred in 28% of patients, with Grade 3 or 4 elevations in 1.8%. Elevated total bilirubin occurred in 6% of patients with Grade 3 or 4 elevations in 0.6%. Liver enzyme elevation can occur with or without concurrent CRS.

Monitor liver enzymes and bilirubin at baseline and during treatment as clinically indicated. Withhold TECVAYLI® or consider permanent discontinuation of TECVAYLI® based on severity.

Infections - TECVAYLI® can cause severe, life-threatening, or fatal infections. In patients who received TECVAYLI® at the recommended dose in the clinical trial, serious infections, including opportunistic infections, occurred in 30% of patients, with Grade 3 or 4 infections in 35%, and fatal infections in 4.2%. Monitor patients for signs and symptoms of infection prior to and during treatment with TECVAYLI® and treat appropriately. Administer prophylactic antimicrobials according to guidelines. Withhold TECVAYLI® or consider permanent discontinuation of TECVAYLI® based on severity.

Monitor immunoglobulin levels during treatment with TECVAYLI® and treat according to guidelines, including infection precautions and antibiotic or antiviral prophylaxis.

Neutropenia - TECVAYLI® can cause neutropenia and febrile neutropenia. In patients who received TECVAYLI® at the recommended dose in the clinical trial, decreased neutrophils occurred in 84% of patients, with Grade 3 or 4 decreased neutrophils in 56%. Febrile neutropenia occurred in 3% of patients.

Monitor complete blood cell counts at baseline and periodically during treatment and provide supportive care per local institutional guidelines. Monitor patients with neutropenia for signs of infection. Withhold TECVAYLI® based on severity.

Hypersensitivity and Other Administration Reactions - TECVAYLI® can cause both systemic administration-related and local injection-site reactions. Systemic Reactions - In patients who received TECVAYLI® at the recommended dose in the clinical trial, 1.2% of patients experienced systemic-administration reactions, which included Grade 1 recurrent pyrexia and Grade 1 swollen tongue. Local Reactions - In patients who received TECVAYLI® at the recommended dose in the clinical trial, injection-site reactions occurred in 35% of patients, with Grade 1 injection-site reactions in 30% and Grade 2 in 4.8%. Withhold TECVAYLI® or consider permanent discontinuation of TECVAYLI® based on severity.

Embryo-Fetal Toxicity - Based on its mechanism of action, TECVAYLI® may cause fetal harm when administered to a pregnant woman. Advise pregnant women of the potential risk to the fetus. Advise females of reproductive potential to use effective contraception during treatment with TECVAYLI® and for 5 months after the last dose.

ADVERSE REACTIONS

The most common adverse reactions (≥20%) were pyrexia, CRS, musculoskeletal pain, injection site reaction, fatigue, upper respiratory tract infection, nausea, headache, pneumonia, and diarrhea. The most common Grade 3 to 4 laboratory abnormalities (≥20%) were decreased lymphocytes, decreased neutrophils, decreased white blood cells, decreased hemoglobin, and decreased platelets.

Please read full Prescribing Information, including Boxed WARNING, for TECVAYLI®.

IMBRUVICA® IMPORTANT SAFETY INFORMATION

INDICATIONS

IMBRUVICA® is a kinase inhibitor indicated for the treatment of:

- Adult patients with chronic lymphocytic leukemia (CLL)/Small lymphocytic lymphoma (SLL).
- Adult patients with chronic lymphocytic leukemia (CLL)/Small lymphocytic lymphoma (SLL) with 17p deletion.

- Adult patients with Waldenström's macroglobulinemia (WM).

- Adult and pediatric patients age 1 year and older with chronic graft versus host disease (cGVHD) after failure of one or more lines of systemic therapy.

For more information, visit www.IMBRUVICA.com.

WARNINGS AND PRECAUTIONS

Hemorrhage: Fatal bleeding events have occurred in patients who received IMBRUVICA®. Major hemorrhage (≥ 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 with B-cell malignancies 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 with B-cell malignancies who received IMBRUVICA® in clinical trials. Grade 3 or greater hypertension occurred in 8% of patients. Based on data from a subset of these patients, (N=1,124), the median time to onset was 5.9 months (range, 0 to 24 months). In a long-term safety analysis over 5 years of 1,284 patients with B-cell malignancies treated for a median of 36 months (range, 0 to 98 months), the cumulative rate of hypertension increased over time. The prevalence for Grade 3 or greater hypertension was 4% (year 0-1), 7% (year 1-2), 9% (year 2-3), 9% (year 3-4), and 9% (year 4-5); the overall incidence for the 5-year period was 11%. 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 with B-cell malignancies who received IMBRUVICA® in clinical trials. The most frequent second primary malignancy was non-melanoma skin cancer (6%).

Hepatotoxicity, Including Drug-Induced Liver Injury: Hepatotoxicity, including severe, life-threatening, and potentially fatal cases of drug-induced liver injury (DILI), has occurred in patients treated with Bruton tyrosine kinase inhibitors, including IMBRUVICA®. Evaluate bilirubin and transaminases at baseline and throughout treatment with IMBRUVICA®. For patients who develop abnormal liver tests after IMBRUVICA®, monitor more frequently for liver test abnormalities and clinical signs and symptoms of hepatic toxicity. If DILI is suspected, withhold IMBRUVICA®. Upon confirmation of DILI, discontinue IMBRUVICA®.

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 (≥30%) in adult patients with B-cell malignancies were thrombocytopenia (55%)*, diarrhea (44%), fatigue (39%), musculoskeletal pain (39%), neutropenia (39%)*, rash (36%), anemia (35%)*, bruising (32%), and nausea (30%).

The most common Grade ≥ 3 adverse reactions (≥5%) in adult patients with B-cell malignancies were neutropenia (21%)*, thrombocytopenia (14%)*, pneumonia (8%), and hypertension (8%).

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

cGVHD: The most common adverse reactions (≥20%) in adult or pediatric patients with cGVHD were fatigue (57%), anemia (49%)*, bruising (40%), diarrhea (36%), thrombocytopenia (33%)*, musculoskeletal pain (30%), pyrexia (30%), muscle spasms (29%), stomatitis (29%), hemorrhage (26%), nausea (26%), abdominal pain (23%), pneumonia (23%), and headache (21%).

The most common Grade 3 or higher adverse reactions (≥5%) reported in adult or pediatric patients with cGVHD were pneumonia (14%), anemia (13%)*, fatigue (12%),

yrexia (11%), diarrhea (10%), neutropenia (10%)*, sepsis (10%), osteonecrosis (9%), stomatitis (9%), hypokalemia (7%), headache (5%), and musculoskeletal pain (5%).

Discontinuation of IMBRUVICA® treatment due to an adverse reaction occurred in 24% of adult patients and 23% of pediatric patients. Adverse reactions leading to dose reduction occurred in 26% of adult patients and 19% of pediatric 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

Pediatric Use: The safety and effectiveness of IMBRUVICA® have not been established for the treatment of cGVHD after failure of one or more lines of therapy in pediatric patients less than 1 year of age. The safety and effectiveness of IMBRUVICA® in pediatric patients have not been established in CLL/SLL, CLL/SLL with 17p deletion, WM, or in patients with mature B-cell non-Hodgkin lymphoma.

In the randomized population from a study that included 35 patients (26 pediatric patients age 5 to less than 17 years) with previously treated mature B-cell non-Hodgkin lymphoma, major hemorrhage and discontinuation of chemoimmunotherapy due to adverse reactions occurred more frequently in the ibrutinib plus chemoimmunotherapy arm compared to the chemoimmunoherapy alone arm.

Hepatic Impairment:

Adult Patients with B-cell Malignancies: 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®.

Patients with cGVHD: Avoid use of IMBRUVICA® in patients with total bilirubin level > 3x upper limit of normal (ULN) (unless of non-hepatic origin or due to Gilbert's syndrome). Reduce recommended dose when administering IMBRUVICA® to patients with total bilirubin level > 1.5 to 3x ULN (unless of non-hepatic origin or due to Gilbert's syndrome).

Please click here to see the full Prescribing Information.

TALVEY® IMPORTANT SAFETY INFORMATION

INDICATION AND USAGE

TALVEY® (talquetamab-tgvs) is indicated for the treatment of adult patients with relapsed or refractory multiple myeloma who have received at least four prior lines of therapy, including a proteasome inhibitor, an immunomodulatory agent, and an anti-CD38 monoclonal antibody.

This indication is approved under accelerated approval based on response rate and durability of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).

IMPORTANT SAFETY INFORMATION

WARNING: CYTOKINE RELEASE SYNDROME and NEUROLOGIC TOXICITY, including IMMUNE EFFECTOR CELL-ASSOCIATED NEUROTOXICITY SYNDROME

Cytokine release syndrome (CRS), including life-threatening or fatal reactions, can occur in patients receiving TALVEY®. Initiate TALVEY® treatment with step-up dosing to reduce the risk of CRS. Withhold TALVEY® until CRS resolves or permanently discontinue based on severity.

Neurologic toxicity, including immune effector cell-associated neurotoxicity syndrome (ICANS), and serious and life-threatening or fatal reactions, can occur with TALVEY®. Monitor patients for signs and symptoms of neurologic toxicity including ICANS during treatment and treat promptly. Withhold or permanently discontinue TALVEY® based on severity.

Because of the risk of CRS and neurologic toxicity, including ICANS, TALVEY® is available only through a restricted program called the TECVAYLI® and TALVEY® Risk Evaluation and Mitigation Strategy (REMS).

CONTRAINDICATIONS: None.

WARNINGS AND PRECAUTIONS

Cytokine Release Syndrome (CRS): TALVEY® can cause cytokine release syndrome, including life-threatening or fatal reactions. In the clinical trial, CRS occurred in 76% of patients who received TALVEY® at the recommended dosages, with Grade 1 CRS occurring in 57% of patients, Grade 2 in 17%, and Grade 3 in 1.5%. Most events occurred following step-up dose 1 (29%) or step-up dose 2 (44%) at the recommended dosages. Recurrent CRS occurred in 30% of patients. CRS occurred in 33% of patients with step-up dose 3 in the biweekly dosing schedule (N=153). CRS occurred in 30% of patients with the first 0.4 mg/kg treatment dose and in 12% of patients treated with the first 0.8 mg/kg treatment dose. The CRS rate for both dosing schedules combined was less than 3% for each of the remaining doses in Cycle 1 and less than 3% cumulatively from Cycle 2 onward. The median time to onset of CRS was 27 (range: 0.1 to 167) hours from the last dose, and the median duration was 17 (range: 0 to 622) hours. Clinical signs and symptoms of CRS include but are not limited to pyrexia, hypotension, chills, hypoxia, headache, and tachycardia. Potentially life-threatening complications of CRS may include cardiac dysfunction, acute respiratory distress syndrome, neurologic toxicity, renal and/or hepatic failure, and disseminated intravascular coagulation (DIC).

Initiate therapy with step-up dosing and administer pre-treatment medications (corticosteroids, antihistamine, and antipyretics) prior to each dose of TALVEY® in the step-up dosing schedule to reduce the risk of CRS. Monitor patients following administration accordingly. In patients who experience CRS, pre-treatment medications should be administered prior to the next TALVEY® dose.

Counsel patients to seek medical attention should signs or symptoms of CRS occur. At the first sign of CRS, immediately evaluate patient for hospitalization and institute treatment with supportive care based on severity, and consider further management per current practice guidelines. Withhold TALVEY® until CRS resolves or permanently discontinue based on severity.

Neurologic Toxicity including ICANS: TALVEY® can cause serious or life-threatening neurologic toxicity, including immune effector cell-associated neurotoxicity syndrome (ICANS), including fatal reactions. In the clinical trial, neurologic toxicity occurred in 55% of patients who received the recommended dosages, with Grade 3 or 4 neurologic toxicity occurring in 6% of patients. The most frequent neurologic toxicities were headache (20%), encephalopathy (15%), sensory neuropathy (14%), and motor dysfunction (10%).

ICANS was reported in 9% of 265 patients where ICANS was collected and who received the recommended dosages. Recurrent ICANS occurred in 3% of patients. Most patients experienced ICANS following step-up dose 1 (3%), step-up dose 2 (3%), step-up dose 3 of the biweekly dosing schedule (1.8%), or the initial treatment dose of the weekly dosing schedule (2.6%) (N=156) or the biweekly dosing schedule (3.7%) (N=109). The median time to onset of ICANS was 2.5 (range: 1 to 16) days after the most recent dose with a median duration of 2 (range: 1 to 22) days. The onset of ICANS can be concurrent with CRS, following resolution of CRS, or in the absence of CRS. Clinical signs and symptoms of ICANS may include but are not limited to confusional state, depressed level of consciousness, disorientation, somnolence, lethargy, and bradyphrenia.

Monitor patients for signs and symptoms of neurologic toxicity during treatment. At the first sign of neurologic toxicity, including ICANS, immediately evaluate the patient and provide supportive care based on severity; withhold or permanently discontinue TALVEY® based on severity and consider further management per current practice guidelines. [see Dosage and Administration (2.5)].

Due to the potential for neurologic toxicity, patients receiving TALVEY® are at risk of depressed level of consciousness. Advise patients to refrain from driving or operating heavy or potentially dangerous machinery during the step-up dosing schedule and for 48 hours after completion of the step-up dosing schedule, and in the event of new onset of any neurological symptoms, until symptoms resolve.

TECVAYLI® and TALVEY® REMS: TALVEY® is available only through a restricted program under a REMS, called the TECVAYLI® and TALVEY® REMS because of the risks of CRS and neurologic toxicity, including ICANS.

Further information about the TECVAYLI® and TALVEY® REMS program is available at www.TEC-TALREMS.com or by telephone at 1-855-810-8064.

Oral Toxicity and Weight Loss: TALVEY® can cause oral toxicities, including dysgeusia, dry mouth, dysphagia, and stomatitis. In the clinical trial, 80% of patients had oral toxicity, with Grade 3 occurring in 2.1% of patients who received the recommended dosages. The most frequent oral toxicities were dysgeusia (49%), dry mouth (34%), dysphagia (23%), and ageusia (18%). The median time to onset of oral toxicity was 15 (range: 1 to 634) days, and the median time to resolution to baseline was 43 (1 to 530) days. Oral toxicity did not resolve to baseline in 65% of patients.

TALVEY® can cause weight loss. In the clinical trial, 62% of patients experienced weight loss of 5% or greater, regardless of having an oral toxicity, including 28% of patients with Grade 2 (10% or greater) weight loss and 2.7% of patients with Grade 3 (20% or greater) weight loss. The median time to onset of Grade 2 or higher weight loss was 67 (range: 6 to 407) days, and the median time to resolution was 50 (range: 1 to 403) days. Weight loss did not resolve in 57% of patients who reported weight loss.

Monitor patients for signs and symptoms of oral toxicity. Counsel patients to seek medical attention should signs or symptoms of oral toxicity occur and provide supportive care as per current clinical practice, including consultation with a nutritionist. Monitor weight regularly during therapy. Evaluate clinically significant weight loss further. Withhold TALVEY® or permanently discontinue based on severity.

Infections: TALVEY® can cause infections, including life-threatening or fatal infections. Serious infections occurred in 16% of patients, with fatal infections in 1.5% of patients. Grade 3 or 4 infections occurred in 17% of patients. The most common serious infections reported were bacterial infection (8%), which included sepsis and COVID-19 (2.7%).

Monitor patients for signs and symptoms of infection prior to and during treatment with TALVEY® and treat appropriately. Administer prophylactic antimicrobials according to local guidelines. Withhold or consider permanently discontinuing TALVEY® as recommended, based on severity.

Cytopenias: TALVEY® can cause cytopenias, including neutropenia and thrombocytopenia. In the clinical trial, Grade 3 or 4 decreased neutrophils occurred in 35% of patients, and Grade 3 or 4 decreased platelets occurred in 22% of patients who received TALVEY®. The median time to onset for Grade 3 or 4 neutropenia was 22 (range: 1 to 312) days, and the median time to resolution to Grade 2 or lower was 8 (range: 1 to 79) days. The median time to onset for Grade 3 or 4 thrombocytopenia was 12 (range: 2 to 183) days, and the median time to resolution to Grade 2 or lower was 10 (range: 1 to 64) days. Monitor complete blood counts during treatment and withhold TALVEY® as recommended, based on severity.

Skin Toxicity: TALVEY® can cause serious skin reactions, including rash, maculo-papular rash, erythema, and erythematous rash. In the clinical trial, skin reactions occurred in 62% of patients, with grade 3 skin reactions in 0.3%. The median time to onset was 25 (range: 1 to 630) days. The median time to improvement to grade 1 or less was 33 days.

Monitor for skin toxicity, including rash progression. Consider early intervention and treatment to manage skin toxicity. Withhold TALVEY® as recommended based on severity.

Hepatotoxicity: TALVEY® can cause hepatotoxicity. Elevated ALT occurred in 33% of patients, with grade 3 or 4 ALT elevation occurring in 2.7%; elevated AST occurred in 31% of patients, with grade 3 or 4 AST elevation occurring in 3.3%. Grade 3 or 4 elevations of total bilirubin occurred in 0.3% of patients. Liver enzyme elevation can occur with or without concurrent CRS.

Monitor liver enzymes and bilirubin at baseline and during treatment as clinically indicated. Withhold TALVEY ® or consider permanent discontinuation of TALVEY®, based on severity [see Dosage and Administration (2.5)].

Embryo-Fetal Toxicity: Based on its mechanism of action, TALVEY® may cause fetal harm when administered to a pregnant woman. Advise pregnant women of the potential risk to the fetus. Advise females of reproductive potential to use effective contraception during treatment with TALVEY® and for 3 months after the last dose.

Adverse Reactions: The most common adverse reactions (≥20%) are pyrexia, CRS, dysgeusia, nail disorder, musculoskeletal pain, skin disorder, rash, fatigue, weight decreased, dry mouth, xerosis, dysphagia, upper respiratory tract infection, diarrhea, hypotension, and headache.

The most common Grade 3 or 4 laboratory abnormalities (≥30%) are lymphocyte count decreased, neutrophil count decreased, white blood cell decreased, and hemoglobin decreased.

Please read full Prescribing Information, including Boxed Warning, for TALVEY®.

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 Johnson & Johnson companies.

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 BALVERSA® (erdafitinib), ERLEADA® (apalutamide), CARVYKTI® (ciltacabtagene autoleucel), TECVAYLI® (teclistamab-cqyv), TALVEY® (talquetamab-tgvs), DARZALEX FASPRO® (daratumumab and hyaluronidase-fihj), DARZALEX® (daratumumab), IMBRUVICA® (ibrutinib) and RYBREVANT® (amivantamab-vmjw) and lazertinib. 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 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; 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 December 31, 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, LLC, Janssen Biotech, Inc. 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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†See the NCCN Guidelines for detailed recommendations, including other treatment options.

§ 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.

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