



NEWS RELEASE

Eisai and Merck Announce Data at 2018 ASCO Annual Meeting from Investigational Studies of LENVIMA® (lenvatinib) and KEYTRUDA® (pembrolizumab) Combination Therapy in Four Different Tumor Types

6/3/2018

First presentation of LENVIMA/KEYTRUDA data in patients with unresectable hepatocellular carcinoma (HCC), which aims to be the first systemic combination of a TKI and immunotherapy for these patients, as well as squamous cell carcinoma of the head and neck (SCCHN)

Updated results show antitumor activity with a consistent safety profile in advanced renal cell carcinoma (RCC) and advanced endometrial carcinoma (EC)

The LENVIMA/KEYTRUDA combination was recently granted U.S. Food and Drug Administration (FDA) Breakthrough Therapy Designation for advanced RCC

Phase 3 trials underway in advanced RCC (NCT02811861) and advanced EC (NCT03517449)

Woodcliff Lake, N.J. & Kenilworth, N.J., June 3, 2018 – Eisai Inc. and Merck (NYSE:MRK), known as MSD outside the United States and Canada, today announced results from presentations of new data and analyses of LENVIMA® (lenvatinib), an orally available kinase inhibitor discovered by Eisai, in combination with Merck's anti-PD-1 therapy, KEYTRUDA® (pembrolizumab), in four different tumor types: unresectable hepatocellular carcinoma (HCC) (Abstract #4076), squamous cell carcinoma of the head and neck (SCCHN) (Abstract #6016), advanced renal cell carcinoma (RCC) (Abstract #4560), and advanced endometrial carcinoma (EC) (Abstract #5596 and Abstract #5597). The data are included in presentations at the 54th Annual Meeting of the American Society of Clinical Oncology (ASCO) in

Chicago from June 1-5. LENVIMA and KEYTRUDA are not approved for use in combination in any cancer types today.

"The data we have observed in the combination studies of LENVIMA plus KEYTRUDA have fueled our commitment to help meet the diverse health care needs of patients living with cancer through clinical studies and research in specific tumor types that are notoriously difficult to treat and continue to have a significant need for new therapeutic options," said Alton Kremer, MD, PhD, Chief Clinical Officer and Chief Medical Officer, Oncology Business Group at Eisai. "We are pleased to share the activity observed in clinical studies of the LENVIMA plus KEYTRUDA combination, as well as rationale for the combination in advanced endometrial carcinoma through translational research."

"With these data at ASCO, we are continuing to see encouraging overall response rates, as well as a safety profile that supports the scientific rationale of adding LENVIMA to KEYTRUDA," said Dr. Roy Baynes, Senior Vice President and Head of Global Clinical Development, Chief Medical Officer, Merck Research Laboratories. "These findings add to the growing body of evidence showing the potential of this combination regimen across a number of tumor types and underscore the strategy behind our collaboration with Eisai."

This release discusses investigational uses for FDA-approved products. It is not intended to convey conclusions about efficacy and safety. There is no guarantee that any investigational uses of FDA-approved products will successfully complete clinical development or gain FDA approval.

Early phase results from Study 116/KEYNOTE-524 support further investigation in unresectable HCC

Study 116/KEYNOTE-524 is a Phase 1b open-label, single-arm multicenter study evaluating the tolerability and safety of the combination of LENVIMA (12 mg/day for patients weighing \geq 60 kg, 8 mg/day for patients weighing < 60 kg) and KEYTRUDA (200 mg intravenously every 3 weeks) in patients with unresectable HCC, Barcelona Clinic Liver Cancer (BCLC) stage B (not eligible for transarterial chemoembolization [TACE]) or C, Child-Pugh class A, and ECOG performance status of 0 or 1. The primary endpoint was safety; secondary and exploratory endpoints included overall survival (OS), objective response rate (ORR), progression-free survival (PFS) and time to progression (TTP) using modified Response Evaluation Criteria in Solid Tumors (mRECIST) criteria. Tumor assessments of complete or partial response (CR or PR) were confirmed greater than or equal to four weeks after initial response. Part 1 evaluated tolerability by assessing dose-limiting toxicities (DLTs) during the first cycle of treatment in patients for whom no other appropriate therapy was available. After tolerability was confirmed, additional patients with no prior systemic therapy for unresectable HCC were enrolled (Part 2). The expansion part of the study will evaluate objective response rate and duration of response as measured by mRECIST.

Data presented at ASCO are from one abstract:

- A Phase 1b trial of lenvatinib (LEN) plus pembrolizumab (PEM) in patients (pts) with unresectable hepatocellular carcinoma (uHCC) (Abstract #4076)

As of March 22, 2018, 30 patients were enrolled in this trial (Part 1, n=6; Part 2, n=24). No dose-limiting toxicities were reported. Four patients discontinued due to treatment emergent adverse events (TEAEs). The most common TEAEs (any grade) were decreased appetite (53.3%) and hypertension (53.3%), diarrhea (43.3%) and fatigue (40.0%). Tumor assessments were performed according to mRECIST by the investigators. At data cutoff, the ORR (including cases of unconfirmed CR and PR) was 42.3% (95% CI: 23.4-63.1). A second scan was performed at least four weeks following the initial response, which demonstrated a confirmed ORR of 26.9% (95% CI: 11.6-47.8). Median duration of PFS was 9.7 months (95% CI: 5.55-NE). None of the treated patients experienced progressive disease (PD) as best overall response (BOR). Twenty-three patients (Part 1, n=3, Part 2, n=20) are still undergoing study treatment. Based on the safety and efficacy data seen thus far, the protocol has been amended to enroll approximately 94 patients to the Part 2 expansion cohort.

New and updated results from Study 111/KEYNOTE-146 support further evaluation in SCCHN, RCC and EC, as well as biomarker analysis with clinical serum samples from patients with advanced EC to clarify combination rationale

Study 111/KEYNOTE-146 is a multicenter, open-label, single-arm Phase 1b/2 basket trial evaluating the combination of LENVIMA (20 mg/day) with KEYTRUDA (200 mg intravenously every three weeks) in patients with selected solid tumors. Patients were not preselected based on PD-L1 status. The primary endpoint of the Phase 1b study was to determine the maximum tolerated dose of KEYTRUDA and LENVIMA in combination. The primary endpoint of the Phase 2 portion is investigator-assessed ORR at week 24 based on immune-related RECIST (irRECIST). The secondary efficacy endpoints included ORR, PFS, and duration of response for patients with complete or partial responses.

Data presented at ASCO are from four abstracts:

- A Phase 1b/2 trial of lenvatinib plus pembrolizumab in patients with squamous cell carcinoma of the head and neck (Abstract #6016)

As of December 1, 2017, 22 patients with measurable, confirmed metastatic SCCHN and ECOG performance status of 0 or 1 were enrolled in this cohort. 90.9% of patients received at least one prior anticancer therapy. At data cutoff, ORR at week 24 was 36.4% (95% CI: 17.2-59.3), overall ORR was 40.9% (including 1 CR and 8 PRs; 95% CI: 20.7-63.6), and PFS rate at 12 months was 41.9% (95% CI: 17.6-64.7). None of the treated patients experienced progressive disease (PD) as best overall response (BOR), and tumor size reduction was observed in the majority of the patients. Grade 3 or 4 TRAEs occurred in 72.7% of patients (Grade 4 TRAEs in 4.5%). The most common TRAEs

(any grade) were fatigue (50.0%), hypertension (40.9%), diarrhea (36.4%), decreased appetite (31.8%), oropharyngeal pain (31.8%) and stomatitis (31.8%). Overall, the study demonstrated promising clinical activity, supporting further evaluation of the combination in patients with SCCHN.

- Lenvatinib + pembrolizumab in patients with renal cell carcinoma: updated results (Abstract #4560)

This cohort enrolled 30 patients with metastatic clear cell RCC and measurable disease per irRECIST. In addition to the assessments performed by investigators per irRECIST, these updated data include tumor assessments performed retrospectively by independent radiographic review (IRR) per irRECIST and RECIST 1.1, as well as the first report of PFS results in this cohort. ORR at week 24 was 63.3% (95% CI: 43.9–80.1), based on investigator assessment per irRECIST. At data cutoff on December 1, 2017, overall ORR was 70.0% (95% CI: 50.6-85.3) based on investigator assessment per irRECIST; median duration of response was 18.4 months (95% CI: 10.3-NE), and median PFS was not estimable (95% CI: 11.6-NE). Based on the IRR per irRECIST, ORR was 66.7% (95% CI: 47.2-82.7), median duration of response was not estimable (95% CI: 14.9-NE), and median PFS was 18.0 months (95% CI: 10.2-NE); per RECIST 1.1, ORR was also 66.7% (95% CI: 47.2-82.7), median duration of response was 16.6 months (95% CI: 8.9-NE), and median PFS was 18.0 months (95% CI: 9.6-NE). Grade 3 or 4 AEs occurred in 22 patients (73.3%), and eight patients (26.7%) discontinued treatment due to an AE. The most common AEs (any grade) were diarrhea (83.3%), fatigue (73.3%), hypothyroidism (70.0%), stomatitis (63.3%) and nausea (60.0%). A Phase 3 trial comparing the LENVIMA plus KEYTRUDA combination and the LENVIMA plus everolimus combination versus sunitinib monotherapy for the first-line treatment of advanced RCC is currently recruiting (CLEAR; NCT02811861; please visit clinicaltrials.gov for more information).

- Lenvatinib + pembrolizumab in patients with advanced endometrial cancer: Updated results (Abstract #5596)

As of data cut-off of December 15, 2017, efficacy and safety analyses are summarized in the poster for 53 patients with histologically confirmed metastatic EC, irrespective of microsatellite instability (MSI) or mismatch repair (MMR) status, and measurable disease per irRECIST. Four (7.5%) patients were MSI-high, 45 (85%) were non MSI-H (MSS), and four (7.5%) patients' MSI status was not known. At data cutoff, ORR at week 24 based on investigator assessment was 39.6% (95% CI: 26.5-54.0); overall ORR was the same. Objective responses were seen regardless of tumor MSI status. Confirmed objective responses were seen in patients with MSS tumors (16/45 [ORR 35.6%]; 95% CI: 21.9-51.2) and MSI-H tumors (2/4 [ORR 50.0%]; 95% CI: 6.8-93.2). Secondary analysis of tumor efficacy by independent radiology review (IRR) showed an ORR at week 24 of 45.3% (95% CI: 31.6-59.6) and an overall ORR of 47.2% (95% CI: 33.3-61.4) with 22 partial responses and three complete responses. Of responding patients, 83.0% (95% CI: 55.9-94.2) had a response duration of six months or more and 64.5% (95% CI: 32.8-84.2) had a response duration of 12 months or more per investigator assessment, and median duration of response had not yet been reached (95% CI: 7.4-NE). When assessed by IRR, among responding patients, 79.3% (95% CI: 48.5-92.9) had a response duration of 12 months or more, and median duration of response was also not yet reached (95% CI: 5.8-

NE). Median PFS was 7.4 months (95% CI: 5.0-not estimable [NE]) per investigator assessment. Most patients showed a decrease in the mean maximum percentage change from baseline in the sum of the diameters of target lesions, regardless of MSI or PD-L1 expression status. Grade 3 treatment-related adverse events (TRAEs) occurred in 37 patients (70%); there were no Grade 4 TRAEs. Five patients (9%) discontinued treatment due to TRAEs. The most common TRAEs (any grade) were hypertension (59%), fatigue (55%), diarrhea (51%), hypothyroidism (47%), decreased appetite (40%), nausea (38%) and stomatitis (34%). A randomized, international, 2-arm, Phase 3 study in recurrent endometrial carcinoma is underway (Study 309/KEYNOTE-775; NCT03517449; please visit clinicaltrials.gov for more information).

- Biomarker results and preclinical rationale for combination of lenvatinib and pembrolizumab in advanced endometrial carcinoma (Abstract #5597)

In an exploratory analysis, 41 candidate serum biomarkers were assessed in immunoassay panels of serum samples collected at baseline, on cycle one, day 15 (C1D15); and cycle two, day one (C2D1) from 37 patients with EC receiving the LENVIMA plus KEYTRUDA combination. In patients with advanced EC, treatment with the combination was associated with changes in several serum biomarkers, including interferon (IFN)- γ and IFN- γ -regulated chemokines, some of which may be associated with tumor response. In addition to the exploratory analysis from Study 111/KEYNOTE-526, preclinical studies on the immunomodulatory and antitumor activity of LENVIMA when combined with PD-1/PD-L1 blockade were presented to more clearly define the basis of combination LENVIMA plus KEYTRUDA. The in vivo preclinical models suggest that LENVIMA monotherapy may decrease the population of tumor-associated macrophage in the tumor microenvironment and the combination therapy may act via a mechanism that includes the interferon signaling pathways to enhance antitumor activity over each monotherapy. Overall, these findings provide rationale for the antitumor activity of LENVIMA plus KEYTRUDA in combination.

About LENVIMA® (lenvatinib) capsules 4 mg and 10 mg

LENVIMA® (lenvatinib) is a kinase inhibitor that is indicated for:

- Differentiated Thyroid Cancer (DTC): single agent for patients with locally recurrent or metastatic, progressive, radioactive iodine-refractory DTC.
- Renal Cell Cancer (RCC): in combination with everolimus for patients with advanced RCC following one prior anti-angiogenic therapy.

Lenvatinib, discovered and developed by Eisai, is a receptor tyrosine kinase (RTK) inhibitor that inhibits the kinase activities of vascular endothelial growth factor (VEGF) receptors VEGFR1 (FLT1), VEGFR2 (KDR), and VEGFR3 (FLT4). Lenvatinib also inhibits other RTKs that have been implicated in pathogenic angiogenesis, tumor growth, and cancer progression in addition to their normal cellular functions, including fibroblast growth factor (FGF) receptors FGFR1-4; the platelet derived growth factor receptor alpha (PDGFR α), KIT, and RET.

Important Safety Information

Warnings and Precautions

- In DTC, hypertension was reported in 73% of patients on LENVIMA vs 16% with placebo (44% vs 4% grade ≥ 3). In RCC, hypertension was reported in 42% of patients on LENVIMA + everolimus vs 10% with everolimus alone (13% vs 2% grade 3). Serious complications of poorly controlled hypertension, including aortic dissection, have been reported. Systolic blood pressure ≥ 160 mmHg occurred in 29% of patients, and 21% of patients had a diastolic blood pressure ≥ 100 mmHg in the LENVIMA + everolimus-treated group. Blood pressure should be controlled prior to treatment and monitored throughout. Withhold dose for grade 3 hypertension despite optimal antihypertensive therapy; resume at reduced dose when controlled at grade ≤ 2 . Discontinue for life-threatening hypertension
- In DTC, cardiac dysfunction was reported in 7% of patients on LENVIMA vs 2% with placebo (2% vs 0% grade ≥ 3). In RCC, decreased ejection fraction and cardiac failure were reported in 10% of patients on LENVIMA + everolimus vs 6% with everolimus alone (3% vs 2% grade 3). Monitor for signs/symptoms of cardiac decompensation. Withhold LENVIMA for development of grade 3 cardiac dysfunction until improvement to grade 0, 1, or baseline. Resume at reduced dose or discontinue based on severity and persistence of cardiac dysfunction. Discontinue for grade 4 cardiac dysfunction
- In DTC, arterial thromboembolic events were reported in 5% of patients on LENVIMA vs 2% with placebo (3% vs 1% grade ≥ 3). In RCC, arterial thromboembolic events were reported in 2% of patients on LENVIMA + everolimus vs 6% with everolimus alone (2% vs 4% grade ≥ 3). Discontinue following an arterial thrombotic event. The safety of resuming LENVIMA after an arterial thromboembolic event has not been established, and LENVIMA has not been studied in patients who have had an arterial thromboembolic event within the previous 6 months
- Across clinical studies in which 1,160 patients received LENVIMA monotherapy, hepatic failure (including fatal events) was reported in 3 patients and acute hepatitis in 1 patient. In DTC, ALT and AST increases (grade ≥ 3) occurred in 4% and 5% of patients on LENVIMA, respectively, vs 0% with placebo. In RCC, ALT and AST increases (grade ≥ 3) occurred in 3% of patients on LENVIMA + everolimus vs 2% and 0% with everolimus alone, respectively. Monitor liver function before initiation, then every 2 weeks for the first 2 months, and at least monthly thereafter during treatment. Withhold dose for liver impairment grade ≥ 3 until resolved to grade 0, 1, or baseline. Resume at reduced dose or discontinue based on severity/persistence of hepatotoxicity. Discontinue for hepatic failure
- In DTC, proteinuria was reported in 34% of patients on LENVIMA vs 3% with placebo (11% vs 0% grade 3). In RCC, proteinuria was reported in 31% of patients on LENVIMA + everolimus vs 14% with everolimus alone (8% vs 2% grade 3). Monitor for proteinuria before and during treatment. Withhold dose for proteinuria ≥ 2 g/24 h. Resume at reduced dose when proteinuria is < 2 g/24 h. Discontinue for nephrotic syndrome

- In RCC, diarrhea was reported in 81% of patients on LENVIMA + everolimus vs 34% with everolimus alone (19% vs 2% grade ≥ 3). Initiate prompt medical management for the development of diarrhea. Monitor for dehydration. Withhold dose for diarrhea grade ≥ 3 . Resume at a reduced dose when diarrhea resolves to grade 1 or baseline. Permanently discontinue LENVIMA for grade 4 diarrhea despite medical management
- In DTC, events of renal impairment were reported in 14% of patients on LENVIMA vs 2% with placebo (3% vs 1% grade ≥ 3). In RCC, events of renal impairment were reported in 18% of patients on LENVIMA + everolimus vs 12% with everolimus alone (10% vs 2% grade ≥ 3). Withhold LENVIMA for grade 3 or 4 renal failure/impairment. Resume at reduced dose or discontinue, depending on severity/persistence of renal impairment. Active management of diarrhea and any other gastrointestinal (GI) symptoms should be initiated for grade 1 events
- In DTC, events of GI perforation or fistula were reported in 2% of patients on LENVIMA vs 0.8% with placebo. In RCC, events of GI perforation, abscess, or fistula (grade ≥ 3) were reported in 2% of patients on LENVIMA + everolimus vs 0% with everolimus alone. Discontinue in patients who develop GI perforation or life-threatening fistula
- In DTC, QT/QTc interval prolongation was reported in 9% of patients on LENVIMA vs 2% with placebo (2% vs 0% >500 ms). In RCC, QTc interval increases >60 ms were reported in 11% of patients on LENVIMA + everolimus (6% >500 ms) vs 0% with everolimus alone. Monitor electrocardiograms in patients with congenital long QT syndrome, congestive heart failure, bradyarrhythmias, or patients taking drugs known to prolong the QT interval. Monitor and correct electrolyte abnormalities in all patients. Withhold dose for QTc interval prolongation >500 ms. Resume at reduced dose when QTc prolongation resolves to baseline
- In DTC, hypocalcemia (grade ≥ 3) was reported in 9% of patients on LENVIMA vs 2% with placebo. In RCC, hypocalcemia (grade ≥ 3) was reported in 6% of patients on LENVIMA + everolimus vs 2% with everolimus alone. Monitor blood calcium levels at least monthly and replace calcium as necessary. Interrupt and adjust LENVIMA as necessary
- Across clinical studies in which 1,160 patients received LENVIMA monotherapy, reversible posterior leukoencephalopathy syndrome (RPLS) was reported in 4 patients. Withhold LENVIMA for RPLS until fully resolved. Resume at reduced dose or discontinue based on the severity and persistence of neurologic symptoms
- Across clinical studies in which 1,160 patients received LENVIMA monotherapy, hemorrhage (grade ≥ 3) was reported in 2% of patients. In DTC, hemorrhagic events occurred in 35% of patients on LENVIMA vs 18% with placebo (2% vs 3% grade ≥ 3). There was 1 fatal intracranial hemorrhage case among 16 patients who received LENVIMA and had central nervous system metastases at baseline. The most frequently reported hemorrhagic event was epistaxis (11% grade 1, 1% grade 2). Discontinuation due to hemorrhagic events occurred in 1% of patients on LENVIMA. In RCC, hemorrhagic events occurred in 34% of patients on LENVIMA + everolimus vs 26% with everolimus alone (8% vs 2% grade ≥ 3). The most frequently reported hemorrhagic event was epistaxis (23% for LENVIMA + everolimus vs 24% with everolimus alone). There was 1 fatal cerebral

hemorrhage case. Discontinuation due to hemorrhagic events occurred in 3% of patients on LENVIMA + everolimus. Consider the risk of severe or fatal hemorrhage associated with tumor invasion/infiltration of major blood vessels (eg, carotid artery). Withhold LENVIMA for the development of grade 3 hemorrhage until resolved to grade 0 or 1. Resume at reduced dose or discontinue based on severity/persistence of hemorrhage. Discontinue for grade 4 hemorrhage

- In DTC patients with normal baseline thyroid-stimulating hormone (TSH), elevation of TSH level above 0.5 mU/L was observed postbaseline in 57% of patients on LENVIMA vs 14% with placebo. In RCC, grade 1 or 2 hypothyroidism occurred in 24% of patients on LENVIMA + everolimus vs 2% with everolimus alone. In RCC patients with normal or low TSH at baseline, elevation of TSH was observed postbaseline in 60% of patients on LENVIMA + everolimus vs 3% with everolimus alone. Monitor thyroid function before initiation of and at least monthly throughout treatment. Treat hypothyroidism according to standard medical practice to maintain a euthyroid state
- Impaired wound healing, including fistula formation, has been reported in patients receiving LENVIMA. Temporary interruption of LENVIMA therapy should be considered in patients undergoing major surgical procedures
- LENVIMA can cause fetal harm when administered to a pregnant woman. Advise females of reproductive potential to use effective contraception during treatment with LENVIMA and for at least

Adverse Reactions

- In DTC, the most common adverse reactions ($\geq 30\%$) observed in LENVIMA-treated patients vs placebo-treated patients were hypertension (73% vs 16%), fatigue (67% vs 35%), diarrhea (67% vs 17%), arthralgia/myalgia (62% vs 28%), decreased appetite (54% vs 18%), weight decrease (51% vs 15%), nausea (47% vs 25%), stomatitis (41% vs 8%), headache (38% vs 11%), vomiting (36% vs 15%), proteinuria (34% vs 3%), palmar-plantar erythrodysesthesia syndrome (32% vs 1%), abdominal pain (31% vs 11%), and dysphonia (31% vs 5%)
- In DTC, adverse reactions led to dose reductions in 68% of patients receiving LENVIMA and in 5% of patients receiving placebo; 18% of patients discontinued LENVIMA and 5% discontinued placebo for adverse reactions. The most common adverse reactions ($\geq 10\%$) resulting in dose reductions of LENVIMA were hypertension (13%), proteinuria (11%), decreased appetite (10%), and diarrhea (10%); the most common adverse reactions ($\geq 1\%$) resulting in discontinuation of LENVIMA were hypertension (1%) and asthenia (1%)
- In RCC, the most common adverse reactions ($>30\%$) observed in patients treated with LENVIMA + everolimus vs everolimus alone were diarrhea (81% vs 34%), fatigue (73% vs 40%), arthralgia/myalgia (55% vs 32%), decreased appetite (53% vs 18%), vomiting (48% vs 12%), nausea (45% vs 16%), stomatitis/oral inflammation (44% vs 50%), hypertension/increased blood pressure (42% vs 10%), peripheral edema (42% vs 20%), cough (37% vs 30%), abdominal pain (37% vs 8%), dyspnea/exertional dyspnea (35% vs 28%), rash (35% vs 40%), weight decreased (34% vs 8%), hemorrhagic events (32% vs 26%), and proteinuria/urine protein present (31%

vs 14%). The most common serious adverse reactions ($\geq 5\%$) were renal failure (11%), dehydration (10%), anemia (6%), thrombocytopenia (5%), diarrhea (5%), vomiting (5%), and dyspnea (5%)

- In RCC, adverse reactions led to dose reductions or interruption in 89% of patients receiving LENVIMA + everolimus and in 54% of patients receiving everolimus alone. The most common adverse reactions ($\geq 5\%$) resulting in dose reductions in the LENVIMA + everolimus-treated group were diarrhea (21%), fatigue (8%), thrombocytopenia (6%), vomiting (6%), nausea (5%), and proteinuria (5%). Treatment discontinuation due to an adverse reaction occurred in 29% of patients in the LENVIMA + everolimus-treated group and in 12% of patients in the everolimus-treated group

Use in Specific Populations

- Because of the potential for serious adverse reactions in nursing infants, advise women to discontinue breastfeeding during treatment
- LENVIMA may result in reduced fertility in females of reproductive potential and may result in damage to male reproductive tissues, leading to reduced fertility of unknown duration

About KEYTRUDA® (pembrolizumab) Injection 100 mg

KEYTRUDA is an anti-PD-1 therapy that works by increasing the ability of the body's immune system to help detect and fight tumor cells. KEYTRUDA is a humanized monoclonal antibody that blocks the interaction between PD-1 and its ligands, PD-L1 and PD-L2, thereby activating T lymphocytes which may affect both tumor cells and healthy cells.

Merck has the industry's largest immuno-oncology clinical research program, which currently involves more than 750 trials studying KEYTRUDA across a wide variety of cancers and treatment settings. The KEYTRUDA clinical program seeks to understand the role of KEYTRUDA across cancers and the factors that may predict a patient's likelihood of benefitting from treatment with KEYTRUDA, including exploring several different biomarkers.

KEYTRUDA (pembrolizumab) Indications and Dosing

Melanoma

KEYTRUDA is indicated for the treatment of patients with unresectable or metastatic melanoma at a fixed dose of 200 mg every three weeks until disease progression or unacceptable toxicity.

Lung Cancer

KEYTRUDA, as a single agent, is indicated for the first-line treatment of patients with metastatic non-small cell lung cancer (NSCLC) whose tumors have high PD-L1 expression [tumor proportion score (TPS) $\geq 50\%$] as determined by

an FDA-approved test, with no EGFR or ALK genomic tumor aberrations.

KEYTRUDA, as a single agent, is also indicated for the treatment of patients with metastatic NSCLC whose tumors express PD-L1 (TPS \geq 1%) as determined by an FDA-approved test, with disease progression on or after platinum-containing chemotherapy. Patients with EGFR or ALK genomic tumor aberrations should have disease progression on FDA-approved therapy for these aberrations prior to receiving KEYTRUDA.

KEYTRUDA, in combination with pemetrexed and carboplatin, is indicated for the first-line treatment of patients with metastatic nonsquamous NSCLC. This indication is approved under accelerated approval based on tumor response rate and progression-free survival. Continued approval for this indication may be contingent upon verification and description of clinical benefit in the confirmatory trials.

In metastatic NSCLC, KEYTRUDA is administered at a fixed dose of 200 mg every three weeks until disease progression, unacceptable toxicity, or up to 24 months in patients without disease progression.

When administering KEYTRUDA in combination with chemotherapy, KEYTRUDA should be administered prior to chemotherapy when given on the same day. See also the Prescribing Information for pemetrexed and carboplatin.

Head and Neck Cancer

KEYTRUDA is indicated for the treatment of patients with recurrent or metastatic head and neck squamous cell carcinoma (HNSCC) with disease progression on or after platinum-containing chemotherapy. This indication is approved under accelerated approval based on tumor response rate and durability of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in the confirmatory trials. In HNSCC, KEYTRUDA is administered at a fixed dose of 200 mg every three weeks until disease progression, unacceptable toxicity, or up to 24 months in patients without disease progression.

Classical Hodgkin Lymphoma

KEYTRUDA is indicated for the treatment of adult and pediatric patients with refractory classical Hodgkin lymphoma (cHL), or who have relapsed after three or more prior lines of therapy. This indication is approved under accelerated approval based on tumor response rate and durability of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in the confirmatory trials. In adults with cHL, KEYTRUDA is administered at a fixed dose of 200 mg every three weeks until disease progression or unacceptable toxicity, or up to 24 months in patients without disease progression. In pediatric patients with cHL, KEYTRUDA is administered at a dose of 2 mg/kg (up to a maximum of 200 mg) every three weeks until disease progression or unacceptable toxicity, or up to 24 months in patients without disease progression.

Urothelial Carcinoma

KEYTRUDA is indicated for the treatment of patients with locally advanced or metastatic urothelial carcinoma who are not eligible for cisplatin-containing chemotherapy. This indication is approved under accelerated approval based on tumor response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in the confirmatory trials.

KEYTRUDA is also indicated for the treatment of patients with locally advanced or metastatic urothelial carcinoma who have disease progression during or following platinum-containing chemotherapy or within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy.

In locally advanced or metastatic urothelial carcinoma, KEYTRUDA is administered at a fixed dose of 200 mg every three weeks until disease progression or unacceptable toxicity, or up to 24 months in patients without disease progression.

Microsatellite Instability-High (MSI-H) Cancer

KEYTRUDA is indicated for the treatment of adult and pediatric patients with unresectable or metastatic microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR)

- solid tumors that have progressed following prior treatment and who have no satisfactory alternative treatment options, or
- colorectal cancer that has progressed following treatment with fluoropyrimidine, oxaliplatin, and irinotecan.

This indication is approved under accelerated approval based on tumor response rate and durability of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in the confirmatory trials. The safety and effectiveness of KEYTRUDA in pediatric patients with MSI-H central nervous system cancers have not been established.

In adult patients with MSI-H cancer, KEYTRUDA is administered at a fixed dose of 200 mg every three weeks until disease progression, unacceptable toxicity, or up to 24 months in patients without disease progression. In children with MSI-H cancer, KEYTRUDA is administered at a dose of 2 mg/kg (up to a maximum of 200 mg) every three weeks until disease progression or unacceptable toxicity, or up to 24 months in patients without disease progression.

Gastric Cancer

KEYTRUDA is indicated for the treatment of patients with recurrent locally advanced or metastatic gastric or

gastroesophageal junction (GEJ) adenocarcinoma whose tumors express PD-L1 [Combined Positive Score (CPS) ≥ 1] as determined by an FDA-approved test, with disease progression on or after two or more prior lines of therapy including fluoropyrimidine- and platinum-containing chemotherapy and if appropriate, HER2/neu-targeted therapy. This indication is approved under accelerated approval based on tumor response rate and durability of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in the confirmatory trials. The recommended dose of KEYTRUDA is 200 mg every three weeks until disease progression, unacceptable toxicity, or up to 24 months in patients without disease progression.

Selected Important Safety Information for KEYTRUDA® (pembrolizumab)

KEYTRUDA can cause immune-mediated pneumonitis, including fatal cases. Pneumonitis occurred in 94 (3.4%) of 2799 patients receiving KEYTRUDA, including Grade 1 (0.8%), 2 (1.3%), 3 (0.9%), 4 (0.3%), and 5 (0.1%) pneumonitis, and occurred more frequently in patients with a history of prior thoracic radiation (6.9%) compared to those without (2.9%). Monitor patients for signs and symptoms of pneumonitis. Evaluate suspected pneumonitis with radiographic imaging. Administer corticosteroids for Grade 2 or greater pneumonitis. Withhold KEYTRUDA for Grade 2; permanently discontinue KEYTRUDA for Grade 3 or 4 or recurrent Grade 2 pneumonitis.

KEYTRUDA can cause immune-mediated colitis. Colitis occurred in 48 (1.7%) of 2799 patients receiving KEYTRUDA, including Grade 2 (0.4%), 3 (1.1%), and 4 (<0.1%) colitis. Monitor patients for signs and symptoms of colitis. Administer corticosteroids for Grade 2 or greater colitis. Withhold KEYTRUDA for Grade 2 or 3; permanently discontinue KEYTRUDA for Grade 4 colitis.

KEYTRUDA can cause immune-mediated hepatitis. Hepatitis occurred in 19 (0.7%) of 2799 patients receiving KEYTRUDA, including Grade 2 (0.1%), 3 (0.4%), and 4 (<0.1%) hepatitis. Monitor patients for changes in liver function. Administer corticosteroids for Grade 2 or greater hepatitis and, based on severity of liver enzyme elevations, withhold or discontinue KEYTRUDA.

KEYTRUDA can cause hypophysitis. Hypophysitis occurred in 17 (0.6%) of 2799 patients receiving KEYTRUDA, including Grade 2 (0.2%), 3 (0.3%), and 4 (<0.1%) hypophysitis. Monitor patients for signs and symptoms of hypophysitis (including hypopituitarism and adrenal insufficiency). Administer corticosteroids and hormone replacement as clinically indicated. Withhold KEYTRUDA for Grade 2; withhold or discontinue for Grade 3 or 4 hypophysitis.

KEYTRUDA can cause thyroid disorders, including hyperthyroidism, hypothyroidism, and thyroiditis. Hyperthyroidism occurred in 96 (3.4%) of 2799 patients receiving KEYTRUDA, including Grade 2 (0.8%) and 3 (0.1%) hyperthyroidism. Hypothyroidism occurred in 237 (8.5%) of 2799 patients receiving KEYTRUDA, including Grade 2 (6.2%) and 3 (0.1%) hypothyroidism. The incidence of new or worsening hypothyroidism was higher in patients with

HNSCC, occurring in 28 (15%) of 192 patients with HNSCC, including Grade 3 (0.5%) hypothyroidism. Thyroiditis occurred in 16 (0.6%) of 2799 patients receiving KEYTRUDA, including Grade 2 (0.3%) thyroiditis. Monitor patients for changes in thyroid function (at the start of treatment, periodically during treatment, and as indicated based on clinical evaluation) and for clinical signs and symptoms of thyroid disorders. Administer replacement hormones for hypothyroidism and manage hyperthyroidism with thionamides and beta-blockers as appropriate. Withhold or discontinue KEYTRUDA for Grade 3 or 4 hyperthyroidism.

KEYTRUDA can cause type 1 diabetes mellitus, including diabetic ketoacidosis, which have been reported in 6 (0.2%) of 2799 patients. Monitor patients for hyperglycemia or other signs and symptoms of diabetes. Administer insulin for type 1 diabetes, and withhold KEYTRUDA and administer antihyperglycemics in patients with severe hyperglycemia.

KEYTRUDA can cause immune-mediated nephritis. Nephritis occurred in 9 (0.3%) of 2799 patients receiving KEYTRUDA, including Grade 2 (0.1%), 3 (0.1%), and 4 (<0.1%) nephritis. Monitor patients for changes in renal function. Administer corticosteroids for Grade 2 or greater nephritis. Withhold KEYTRUDA for Grade 2; permanently discontinue KEYTRUDA for Grade 3 or 4 nephritis.

Immune-mediated rashes, including Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN) (some cases with fatal outcome), exfoliative dermatitis, and bullous pemphigoid, can occur. Monitor patients for suspected severe skin reactions and based on the severity of the adverse reaction, withhold or permanently discontinue KEYTRUDA and administer corticosteroids. For signs or symptoms of SJS or TEN, withhold KEYTRUDA and refer the patient for specialized care for assessment and treatment. If SJS or TEN is confirmed, permanently discontinue KEYTRUDA.

KEYTRUDA can cause other clinically important immune-mediated adverse reactions. These immune-mediated reactions may occur in any organ system. For suspected immune-mediated adverse reactions, ensure adequate evaluation to confirm etiology or exclude other causes. Based on the severity of the adverse reaction, withhold KEYTRUDA and administer corticosteroids. Upon improvement to Grade 1 or less, initiate corticosteroid taper and continue to taper over at least 1 month. Based on limited data from clinical studies in patients whose immune-related adverse reactions could not be controlled with corticosteroid use, administration of other systemic immunosuppressants can be considered. Resume KEYTRUDA when the adverse reaction remains at Grade 1 or less following corticosteroid taper. Permanently discontinue KEYTRUDA for any Grade 3 immune-mediated adverse reaction that recurs and for any life-threatening immune-mediated adverse reaction.

The following clinically significant immune-mediated adverse reactions occurred in less than 1% (unless otherwise indicated) of 2799 patients: arthritis (1.5%), uveitis, myositis, Guillain-Barré syndrome, myasthenia gravis, vasculitis, pancreatitis, hemolytic anemia, and partial seizures arising in a patient with inflammatory foci in brain parenchyma.

In addition, myelitis and myocarditis were reported in other clinical trials, including classical Hodgkin lymphoma, and postmarketing use.

Solid organ transplant rejection has been reported in postmarketing use of KEYTRUDA. Treatment with KEYTRUDA may increase the risk of rejection in solid organ transplant recipients. Consider the benefit of treatment with KEYTRUDA vs the risk of possible organ rejection in these patients.

KEYTRUDA can cause severe or life-threatening infusion-related reactions, including hypersensitivity and anaphylaxis, which have been reported in 6 (0.2%) of 2799 patients. Monitor patients for signs and symptoms of infusion-related reactions, including rigors, chills, wheezing, pruritus, flushing, rash, hypotension, hypoxemia, and fever. For Grade 3 or 4 reactions, stop infusion and permanently discontinue KEYTRUDA.

Immune-mediated complications, including fatal events, occurred in patients who underwent allogeneic hematopoietic stem cell transplantation (HSCT) after being treated with KEYTRUDA. Of 23 patients with cHL who proceeded to allogeneic HSCT after treatment with KEYTRUDA on any trial, 6 patients (26%) developed graft-versus-host disease (GVHD), one of which was fatal, and 2 patients (9%) developed severe hepatic veno-occlusive disease (VOD) after reduced-intensity conditioning, one of which was fatal. Cases of fatal hyperacute GVHD after allogeneic HSCT have also been reported in patients with lymphoma who received a PD-1 receptor–blocking antibody before transplantation.

These complications may occur despite intervening therapy between PD-1 blockade and allogeneic HSCT. Follow patients closely for early evidence of transplant-related complications such as hyperacute GVHD, severe (Grade 3 to 4) acute GVHD, steroid-requiring febrile syndrome, hepatic VOD, and other immune-mediated adverse reactions, and intervene promptly.

In clinical trials in patients with multiple myeloma, the addition of KEYTRUDA to a thalidomide analogue plus dexamethasone resulted in increased mortality. Treatment of these patients with a PD-1 or PD-L1 blocking antibody in this combination is not recommended outside of controlled clinical trials.

Based on its mechanism of action, KEYTRUDA can cause fetal harm when administered to a pregnant woman. If used during pregnancy, or if the patient becomes pregnant during treatment, apprise the patient of the potential hazard to a fetus. Advise females of reproductive potential to use highly effective contraception during treatment and for 4 months after the last dose of KEYTRUDA.

In KEYNOTE-006, KEYTRUDA was discontinued due to adverse reactions in 9% of 555 patients with advanced melanoma; adverse reactions leading to discontinuation in more than one patient were colitis (1.4%), autoimmune hepatitis (0.7%), allergic reaction (0.4%), polyneuropathy (0.4%), and cardiac failure (0.4%). Adverse reactions leading

to interruption of KEYTRUDA occurred in 21% of patients; the most common ($\geq 1\%$) was diarrhea (2.5%). The most common adverse reactions with KEYTRUDA vs ipilimumab were fatigue (28% vs 28%), diarrhea (26% with KEYTRUDA), rash (24% vs 23%), and nausea (21% with KEYTRUDA). Corresponding incidence rates are listed for ipilimumab only for those adverse reactions that occurred at the same or lower rate than with KEYTRUDA.

In KEYNOTE-010, KEYTRUDA monotherapy was discontinued due to adverse reactions in 8% of 682 patients with metastatic NSCLC. The most common adverse event resulting in permanent discontinuation of KEYTRUDA was pneumonitis (1.8%). Adverse reactions leading to interruption of KEYTRUDA occurred in 23% of patients; the most common ($\geq 1\%$) were diarrhea (1%), fatigue (1.3%), pneumonia (1%), liver enzyme elevation (1.2%), decreased appetite (1.3%), and pneumonitis (1%). The most common adverse reactions (occurring in at least 20% of patients and at a higher incidence than with docetaxel) were decreased appetite (25% vs 23%), dyspnea (23% vs 20%), and nausea (20% vs 18%).

In KEYNOTE-021(G1), when KEYTRUDA was administered in combination with carboplatin and pemetrexed (carbo/pem) in advanced nonsquamous NSCLC, KEYTRUDA was discontinued in 10% of 59 patients. The most common adverse reaction resulting in discontinuation of KEYTRUDA ($\geq 2\%$) was acute kidney injury (3.4%). Adverse reactions leading to interruption of KEYTRUDA occurred in 39% of patients; the most common ($\geq 2\%$) were fatigue (8%), neutrophil count decreased (8%), anemia (5%), dyspnea (3.4%), and pneumonitis (3.4%). The most common adverse reactions ($\geq 20\%$) with KEYTRUDA compared to carbo/pem alone were fatigue (71% vs 50%), nausea (68% vs 56%), constipation (51% vs 37%), rash (42% vs 21%), vomiting (39% vs 27%), dyspnea (39% vs 21%), diarrhea (37% vs 23%), decreased appetite (31% vs 23%), headache (31% vs 16%), cough (24% vs 18%), dizziness (24% vs 16%), insomnia (24% vs 15%), pruritus (24% vs 4.8%), peripheral edema (22% vs 18%), dysgeusia (20% vs 11%), alopecia (20% vs 3.2%), upper respiratory tract infection (20% vs 3.2%), and arthralgia (15% vs 24%). This study was not designed to demonstrate a statistically significant difference in adverse reaction rates for KEYTRUDA as compared to carbo/pem alone for any specified adverse reaction.

In KEYNOTE-012, KEYTRUDA was discontinued due to adverse reactions in 17% of 192 patients with HNSCC. Serious adverse reactions occurred in 45% of patients. The most frequent serious adverse reactions reported in at least 2% of patients were pneumonia, dyspnea, confusional state, vomiting, pleural effusion, and respiratory failure. The most common adverse reactions (reported in at least 20% of patients) were fatigue, decreased appetite, and dyspnea. Adverse reactions occurring in patients with HNSCC were generally similar to those occurring in patients with melanoma or NSCLC, with the exception of increased incidences of facial edema (10% all Grades; 2.1% Grades 3 or 4) and new or worsening hypothyroidism.

In KEYNOTE-087, KEYTRUDA was discontinued due to adverse reactions in 5% of 210 patients with cHL, and treatment was interrupted due to adverse reactions in 26% of patients. Fifteen percent (15%) of patients had an

adverse reaction requiring systemic corticosteroid therapy. Serious adverse reactions occurred in 16% of patients. The most frequent serious adverse reactions ($\geq 1\%$) included pneumonia, pneumonitis, pyrexia, dyspnea, GVHD, and herpes zoster. Two patients died from causes other than disease progression; one from GVHD after subsequent allogeneic HSCT and one from septic shock. The most common adverse reactions (occurring in $\geq 20\%$ of patients) were fatigue (26%), pyrexia (24%), cough (24%), musculoskeletal pain (21%), diarrhea (20%), and rash (20%).

In KEYNOTE-052, KEYTRUDA was discontinued due to adverse reactions in 11% of 370 patients with locally advanced or metastatic urothelial carcinoma. The most common adverse reactions (in $\geq 20\%$ of patients) were fatigue (38%), musculoskeletal pain (24%), decreased appetite (22%), constipation (21%), rash (21%), and diarrhea (20%). Eighteen patients (5%) died from causes other than disease progression. Five patients (1.4%) who were treated with KEYTRUDA experienced sepsis which led to death, and 3 patients (0.8%) experienced pneumonia which led to death. Adverse reactions leading to interruption of KEYTRUDA occurred in 22% of patients; the most common ($\geq 1\%$) were liver enzyme increase, diarrhea, urinary tract infection, acute kidney injury, fatigue, joint pain, and pneumonia. Serious adverse reactions occurred in 42% of patients, the most frequent ($\geq 2\%$) of which were urinary tract infection, hematuria, acute kidney injury, pneumonia, and urosepsis.

In KEYNOTE-045, KEYTRUDA was discontinued due to adverse reactions in 8% of 266 patients with locally advanced or metastatic urothelial carcinoma. The most common adverse reaction resulting in permanent discontinuation of KEYTRUDA was pneumonitis (1.9%). Adverse reactions leading to interruption of KEYTRUDA occurred in 20% of patients; the most common ($\geq 1\%$) were urinary tract infection (1.5%), diarrhea (1.5%), and colitis (1.1%). The most common adverse reactions ($\geq 20\%$) in patients who received KEYTRUDA vs those who received chemotherapy were fatigue (38% vs 56%), musculoskeletal pain (32% vs 27%), pruritus (23% vs 6%), decreased appetite (21% vs 21%), nausea (21% vs 29%), and rash (20% vs 13%). Serious adverse reactions occurred in 39% of KEYTRUDA-treated patients, the most frequent ($\geq 2\%$) of which were urinary tract infection, pneumonia, anemia, and pneumonitis.

It is not known whether KEYTRUDA is excreted in human milk. Because many drugs are excreted in human milk, instruct women to discontinue nursing during treatment with KEYTRUDA and for 4 months after the final dose.

There is limited experience in pediatric patients. In a study, 40 pediatric patients (16 children aged 2 years to younger than 12 years and 24 adolescents aged 12 years to 18 years) with advanced melanoma, lymphoma, or PD-L1-positive advanced, relapsed, or refractory solid tumors were administered KEYTRUDA 2 mg/kg every 3 weeks. Patients received KEYTRUDA for a median of 3 doses (range 1–17 doses), with 34 patients (85%) receiving KEYTRUDA for 2 doses or more. The safety profile in these pediatric patients was similar to that seen in adults treated with KEYTRUDA. Toxicities that occurred at a higher rate ($\geq 15\%$ difference) in these patients when compared to adults under 65 years of age were fatigue (45%), vomiting (38%), abdominal pain (28%), hypertransaminasemia (28%), and hyponatremia (18%).

About the Eisai and Merck Strategic Collaboration

In March 2018, Eisai and Merck, through an affiliate, entered into a strategic collaboration for the worldwide co-development and co-commercialization of LENVIMA. Under the agreement, the companies will develop and commercialize LENVIMA jointly, both as monotherapy and in combination with Merck's anti-PD-1 therapy. In addition to ongoing clinical studies of the combination, the companies will jointly initiate new clinical studies evaluating the combination to support 11 potential indications in six types of cancer (bladder cancer, endometrial cancer, head and neck cancer, hepatocellular carcinoma, melanoma, and non-small cell lung cancer), as well as a basket trial targeting six additional cancer types. The combination is not approved in any cancer types today.

About Eisai Inc.

At Eisai Inc., human health care (hhc) is our goal. We give our first thoughts to patients and their families, and helping to increase the benefits health care provides. As the U.S. pharmaceutical subsidiary of Tokyo-based Eisai Co., Ltd., we have a passionate commitment to patient care that is the driving force behind our efforts to discover and develop innovative therapies to help address unmet medical needs.

Eisai is a fully integrated pharmaceutical business that operates in two global business groups: oncology and neurology (dementia-related diseases and neurodegenerative diseases). Each group functions as an end-to-end global business with discovery, development, manufacturing and marketing capabilities. Our U.S. headquarters, commercial and clinical development organizations are located in New Jersey; our discovery labs are in Massachusetts and Pennsylvania; and our global demand chain organization resides in Maryland and North Carolina. To learn more about Eisai Inc., please visit us at eisai.com/us.

Merck's Focus on Cancer

Our goal is to translate breakthrough science into innovative oncology medicines to help people with cancer worldwide. At Merck, the potential to bring new hope to people with cancer drives our purpose and supporting accessibility to our cancer medicines is our commitment.

As part of our focus on cancer, Merck is committed to exploring the potential of immuno-oncology with one of the largest development programs in the industry across more than 30 tumor types. We also continue to strengthen our portfolio through strategic acquisitions and are prioritizing the development of several promising oncology candidates with the potential to improve the treatment of advanced cancers.

For more information about our oncology clinical trials, visit www.merck.com/clinicaltrials.

About Merck

For more than a century, Merck, a leading global biopharmaceutical company known as MSD outside of the United States and Canada, has been inventing for life, bringing forward medicines and vaccines for many of the world's most challenging diseases. Through our prescription medicines, vaccines, biologic therapies and animal health products, we work with customers and operate in more than 140 countries to deliver innovative health solutions. We also demonstrate our commitment to increasing access to health care through far-reaching policies, programs and partnerships. Today, Merck continues to be at the forefront of research to advance the prevention and treatment of diseases that threaten people and communities around the world - including cancer, cardio-metabolic diseases, emerging animal diseases, Alzheimer's disease and infectious diseases including HIV and Ebola. For more information, visit www.merck.com and connect with us on [Twitter](#), [Facebook](#), [Instagram](#), [YouTube](#) and [LinkedIn](#).

Forward-Looking Statement of Merck & Co., Inc., Kenilworth, N.J., USA

This news release of Merck & Co., Inc., Kenilworth, N.J., USA (the "company") includes "forward-looking statements" within the meaning of the safe harbor provisions of the U.S. Private Securities Litigation Reform Act of 1995. These statements are based upon the current beliefs and expectations of the company's management and are subject to significant risks and uncertainties. There can be no guarantees with respect to pipeline products that the products will receive the necessary regulatory approvals or that they will prove to be commercially successful. If underlying assumptions prove inaccurate or risks or uncertainties materialize, actual results may differ materially from those set forth in the forward-looking statements.

Risks and uncertainties include but are not limited to, general industry conditions and competition; general economic factors, including interest rate and currency exchange rate fluctuations; the impact of pharmaceutical industry regulation and health care legislation in the United States and internationally; global trends toward health care cost containment; technological advances, new products and patents attained by competitors; challenges inherent in new product development, including obtaining regulatory approval; the company's ability to accurately predict future market conditions; manufacturing difficulties or delays; financial instability of international economies and sovereign risk; dependence on the effectiveness of the company's patents and other protections for innovative products; and the exposure to litigation, including patent litigation, and/or regulatory actions.

The company undertakes no obligation to publicly update any forward-looking statement, whether as a result of new information, future events or otherwise. Additional factors that could cause results to differ materially from those described in the forward-looking statements can be found in the company's 2017 Annual Report on Form 10-K and the company's other filings with the Securities and Exchange Commission (SEC) available at the SEC's Internet site (www.sec.gov).

Please see Prescribing Information for LENVIMA (lenvatinib) at <http://www.lenvima.com/pdfs/prescribing-information.pdf>

Please see Prescribing Information for KEYTRUDA (pembrolizumab) at http://www.merck.com/product/usa/pi_circulars/k/keytruda/keytruda_pi.pdf and Patient Information/Medication Guide for KEYTRUDA at http://www.merck.com/product/usa/pi_circulars/k/keytruda/keytruda_mg.pdf

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