ANDREW MCCARTHY





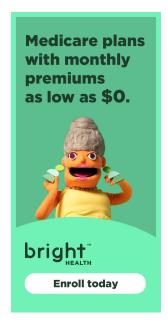






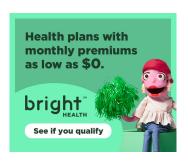
Plan on saving hundreds on a health plan. Then plan a party.

















of-office to "enjoying a business flight."

Do business travel right.







• APTIV



· APTIV •

Logo

The Aptiv Logo

The Aptiv visual identity embodies our company's innovative spirit.
Our logo is an essential brand asset that must be protected through consistent and conscientious usage as specified in these guidelines.

Our logo files are available to download from the Aptiv Marketing Communications Sharepoint at this address:

http://s01.delphiauto.net/01/mcs/ SitePages/index_page.aspx

Clear Space





The measurements and proportions of our logo should not be modified or altered.

Always ensure the logo is legible and shown at or larger than the minimum size.



Points: Usage

- · Points must be used sparingly to preserve the integrity of their meaning.
- Points can be displayed as either whole- or half-points.
- In the presence of our logo, use only one point on a page This prevents visual redundancy. If there is no logo on a page, dual points may be used.
- Align and position points in relation to either the top or bottom of a text block/color block. See examples shown.



Clear space around points should be equal to at least the diameter of one point. Half points should be aligned to the cap height of any large title copy.

If there is no large title text to base point size on, use quarter increments of the logo height (100%, 75%, 50%, etc.)



Example layout with point sized to cap height and aligned at bottom of content

Example layout with point sized to 100% of logo height and aligned at top of content

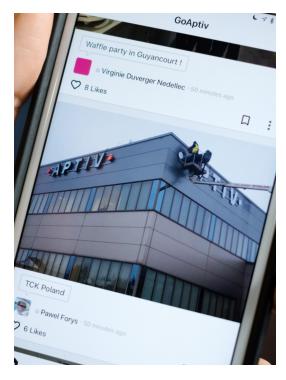














































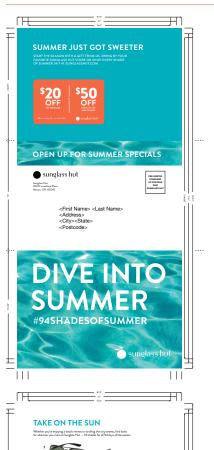














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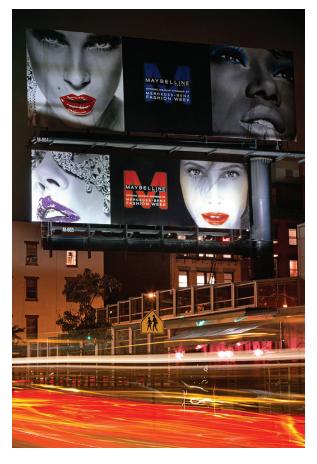








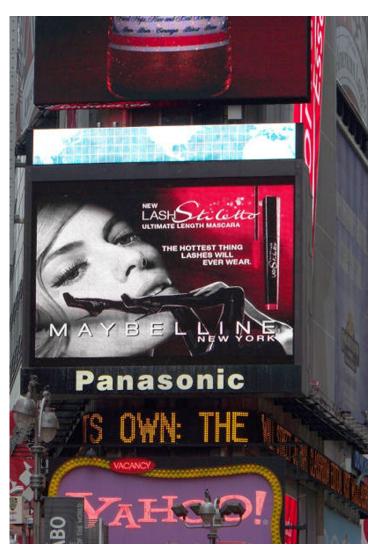






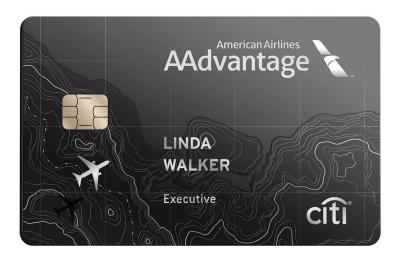






















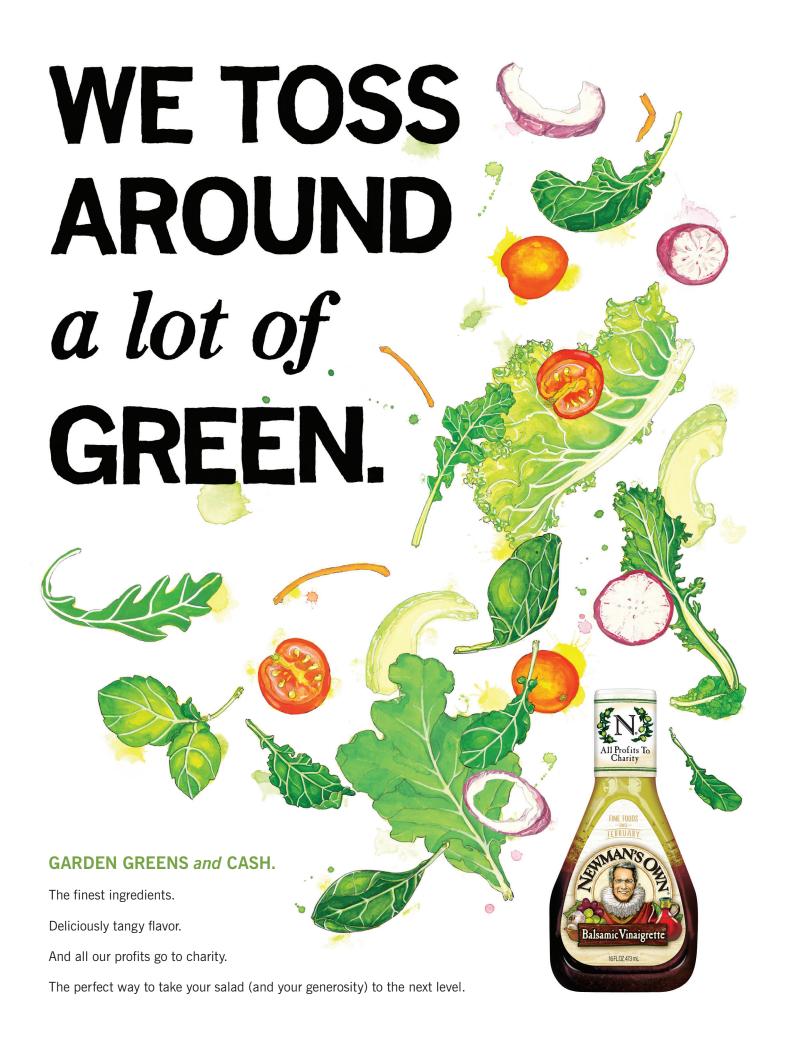












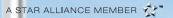














With MySkyStatus, in-the-air doesn't mean out-of-touch.

Fly from 17 U.S. gateways to more than 400 worldwide destinations and never leave your friends behind. Post departure and arrival info and set in-flight updates from your smartphone at MySkyStatus.com and alerts will be sent via Facebook and Twitter.



There's no better way to fly." **Lufthansa**

















XALKORI® (crizotinib) 250 mg capsules is an oral medicine that inhibits the anaplastic lymphoma kinase (ALK) and ROS1 receptor tyrosine kinases.^{1,2}

XALKORI was the first ALK inhibitor approved in the U.S. and is indicated for the treatment of patients with metastatic non-small cell lung cancer (NSCLC) whose tumors are ALK-positive as detected by an FDA-approved test.

XALKORI is also the first and only FDA-approved biomarker-driven therapy indicated for the treatment of patients with metastatic NSCLC whose tumors are ROS1-positive.

To date, over 10,000 patients have been treated with XALKORI in the U.S.³

ALK IN LUNG CANCER

Originally discovered as an oncogenic driver in a type of lymphoma, ALK gene alterations were also found to be among key drivers of tumor development in cancers such as NSCLC and rare sarcomas. By inhibiting ALK, XALKORI blocks signaling in a number of cell pathways that are believed to be critical for the growth and survival of tumor cells. ALK, and the survival of tumor cells.

In ALK-positive lung cancer, a normally dormant gene named ALK is fused with another gene, predominantly EML4. This genetic alteration creates the ALK fusion gene and ultimately, the production of the ALK fusion protein, which is responsible for tumor growth.^{4,5} Epidemiology studies suggest that approximately 3 to 5 percent of NSCLC tumors are ALK-positive.⁶

Only biomarker testing can determine which patients have ALK-positive metastatic NSCLC. In the U.S., the Vysis ALK Break Apart FISH Probe Kit (Abbott Molecular) and the Ventana ALK (D5F3) CDx Assay are the only FDA-approved tests for detecting ALK.

ROS1 IN LUNG CANCER

Another gene that can rearrange or combine with other genes is called ROS1. Sometimes the ROS1 gene can attach to another gene, changing the way each gene normally functions. This ROS1 gene rearrangement can contribute to cancer-cell growth and tumor survival. This change occurs in approximately one percent of NSCLC cases. Of the estimated 1.5 million new cases of NSCLC worldwide each year, roughly 15,000 may be driven by oncogenic ROS1 fusions.^{7,8,9}

An FDA-approved test for the detection of ROS1 rearrangements in NSCLC is not currently available; however, laboratory developed tests are available. A companion diagnostic test is currently under development to identify patients with ROS1-positive metastatic NSCLC who may benefit from treatment with XALKORI.

NSCLC CLINICAL STUDIES

PROFILE 1014 studied XALKORI 250 mg twice daily in previously untreated patients with ALK-positive metastatic NSCLC versus standard platinum-based chemotherapy regimens. This Phase 3 study enrolled 343 participants from clinical sites globally. Patients in the chemotherapy arm of the study received one of the following standard-of-care chemotherapy regimens based on the choice of the investigator: either pemetrexed 500 mg/m² with cisplatin 75 mg/m² or carboplatin AUC of 5 or 6 min/mL by intravenous infusion every 3 weeks for up to 6 cycles. Patients were required to have ALK-positive NSCLC, as identified by the FDA-approved assay Vysis ALK Break Apart FISH Probe Kit, prior to randomization.

- In PROFILE 1014, XALKORI demonstrated significantly prolonged progression-free survival (PFS) of 10.9 months (95 % CI, 8.3 to 13.9) (n=172) compared to 7.0 months (95 % CI, 6.8 to 8.2) with chemotherapy (n=171) in previously untreated patients with ALK-positive metastatic NSCLC (hazard ratio, 0.45; 95 % CI: 0.35 to 0.60; P<0.001).
- XALKORI also demonstrated significantly higher objective response rate (ORR) when compared to standard platinum-based chemotherapy regimens. XALKORI demonstrated an ORR of 74% (95% CI, 67 to 81) compared to an ORR of 45% (95% CI, 37 to 53) for the chemotherapy arm (*P*<0.001).





IBRANCE is indicated for the treatment of hormone receptor-positive (HR+), human epidermal growth factor receptor 2-negative (HER2-) advanced or metastatic breast cancer in combination with:

- an aromatase inhibitor as initial endocrine-based therapy in postmenopausal women; or
- fulvestrant in women with disease progression following endocrine therapy.¹

ABOUT IBRANCE® (palbociclib)

IBRANCE is a selective oral inhibitor of CDKs 4 and 6.1 CDKs 4 and 6 are key regulators of the cell cycle that trigger cellular progression.^{2,3}

IBRANCE is the first CDK 4/6 inhibitor approved by the U.S. Food and Drug Administration (FDA). IBRANCE was reviewed and approved under the FDA's Breakthrough Therapy designation and Priority Review programs.

IBRANCE was discovered and is marketed by Pfizer Inc. For more information, please visit www.IBRANCE.com.

TARGETING CDKS 4 AND 6 IN CANCER

CDKs are a family of proteins that serve as key regulators of cell growth and division. Specifically, cyclins pair with CDKs 4 and 6 to take part in a fundamental process in the division of cells, called the cell cycle.^{2,3} This occurs in both normal and cancer cells and is composed of four phases:^{2,3}

- G1: This phase marks the beginning of the cell cycle, where the raw material is built and prepared for the S phase^{2,3}
- S: DNA, or the vital information instructing the function of the cell, is constructed³
- G2: The cell begins to grow and prepares for mitosis²
- M: The cell cycle is completed and the cell splits into two genetically alike daughter cells³

CDKs 4 and 6 are key regulators of the cell cycle that trigger progression through G1 to the S phase. $^{2.3}$ In some cancers, including HR+ breast cancer, increased activity of the cyclin D1-CDK 4/6-complex may result in a failure to regulate cell proliferation. $^{2.4,5}$ Inhibiting CDKs 4 and 6 may help reduce cellular proliferation of HR+ breast cancer cell lines. 1 CDK 4/6 is also active in healthy cells. Inhibiting CDK 4/6 in healthy cells can result in side effects, some of which may be serious. 1

IMPORTANT SAFETY INFORMATION

Neutropenia was the most frequently reported adverse reaction in PALOMA-2 (80%) and PALOMA-3 (83%). In PALOMA-2, Grade 3 (56%) or 4 (10%) decreased neutrophil counts were reported in patients receiving IBRANCE plus letrozole. In PALOMA-3, Grade 3 (55%) or Grade 4 (11%) decreased neutrophil counts were reported in patients receiving IBRANCE plus fulvestrant. Febrile neutropenia has been reported in 1.8% of patients exposed to IBRANCE across PALOMA-2 and PALOMA-3. One death due to neutropenic sepsis was observed in PALOMA-3. Inform patients to promptly report any fever.

Monitor complete blood count prior to starting IBRANCE, at the beginning of each cycle, on Day 15 of first 2 cycles and as clinically indicated. Dose interruption, dose reduction, or delay in starting treatment cycles is recommended for patients who develop Grade 3 or 4 neutropenia.

Based on the mechanism of action, IBRANCE can cause **fetal harm**. Advise females of reproductive potential to use effective contraception during IBRANCE treatment and for at least 3 weeks after the last dose. IBRANCE may **impair fertility in males** and has the potential to cause genotoxicity. Advise male patients with female partners of reproductive potential to use effective contraception during IBRANCE treatment and for 3 months after the last dose. Advise females to inform their healthcare provider of a known or suspected pregnancy. Advise women **not to breastfeed** during IBRANCE treatment and for 3 weeks after the last dose because of the potential for serious adverse reactions in nursing infants.

Important Safety Information continued on page 2



