ANDREW McCARTHY

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.[4] 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.[4,5]

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.[10] 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/m^2 with cisplatin 75 mg/m^2 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).

PP-XLK-USA-0538 March 2017

IBRANCE™
palbociclib | 125 mg capsules

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 constructed[3]
- *G2*: The cell begins to grow and prepares for mitosis[2]
- *M*: The cell cycle is completed and the cell splits into two genetically alike daughter cells[3]

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

KEY MILESTONES IN THE HISTORY & DEVELOPMENT OF IBRANCE® (PALBOCICLIB) IN BREAST CANCER

1990

Cyclin-dependent kinases (CDKs) are identified as key regulators of cell growth and division, a significant scientific discovery.[14] Cancer researchers begin exploring the treatment potential of CDK inhibition, but note the toxicity of pan-CDK inhibitors in the clinic.[14]

1995-2001

Pfizer researchers in Ann Arbor, Michigan, discover the compound palbociclib, a selective inhibitor of CDKs 4 and 6, as part of a multi-year research collaboration with Onyx Pharmaceuticals (now a subsidiary of Amgen).

2001

Three UK researchers – Sir Paul Nurse, Tim Hunt and Leland Hartwell – are awarded the Nobel Prize for their work uncovering the role of CDKs in the cell cycle.[15]

2002

Pfizer's Oncology Research Unit selects palbociclib as its lead CDK inhibitor because of its ability to selectively target CDKs 4 and 6, key regulators of the cell cycle that trigger cellular progression.

2004-2007

Palbociclib enters Phase 1 clinical trials and the first patient is treated.

Multiple clinical studies are conducted to investigate the safety and anti-tumor activity of palbociclib. While these studies add to the scientific understanding of the compound, they do not demonstrate a strong clinical signal of efficacy for palbociclib in unselected patient populations.

2007

Pfizer researchers in La Jolla, California, begin collaborating with translational oncology scientists at UCLA's Jonsson Comprehensive Cancer Center, including pioneer breast cancer researcher Dr. Dennis Slamon, and clear signals of differentiated activity in pre-clinical models of models of ER+ breast cancer are identified.[16]

2008

SEPTEMBER: The first patient is dosed in the Phase 1 portion of PALOMA-1, the Phase 1/2 study evaluating palbociclib in combination with letrozole in ER+/human epidermal growth factor receptor 2 negative (HER2-) advanced breast cancer.[18]

2009

DECEMBER: The Phase 2 portion of PALOMA-1 is initiated.[18]

2012

MARCH: Pfizer demonstrates proof of concept for palbociclib, showing that the compound is active in patients with ER+/HER2- breast cancer.

DECEMBER: PALOMA-1 lead investigator Dr. Richard Finn presents interim results from the study at the 2012 CTRC-AACR San Antonio Breast Cancer Symposium (SABCS).[16]

2013

FEBRUARY: Pfizer initiates PALOMA-2, a global Phase 3 trial in the same population of women as PALOMA-1.[6]

APRIL: Palbociclib is granted Breakthrough Therapy designation by the U.S. Food and Drug Administration (FDA).

SEPTEMBER: PALOMA-3 was initiated to evaluate the efficacy and safety profile of palbociclib plus fulvestrant in pre-, peri- and post-menopausal women with HR+/HER2- metastatic breast cancer whose disease progressed on or after prior endocrine therapy in the adjuvant or metastatic setting.[8]

NOVEMBER: An additional global Phase 3 trial, PENELOPE-B, evaluating palbociclib in HR+/HER2- early breast cancer is initiated, led by the German Breast Group (GBG).[10]

2014

FEBRUARY: Pfizer announces positive top-line results from PALOMA-1, which demonstrate that adding palbociclib to letrozole prolongs PFS over letrozole alone.

APRIL: Dr. Richard Finn presents detailed results from PALOMA-1 at the American Association of Cancer Research (AACR) Annual Meeting 2014 in San Diego.

OCTOBER: On October 13, which is Metastatic Breast Cancer Awareness Day, Pfizer announces that its New Drug Application for palbociclib has been accepted for filing and granted Priority Review by the FDA.

2015

JANUARY: Results from PALOMA-1 are published in *The Lancet Oncology.*[19]

FEBRUARY: Pfizer receives accelerated approval of IBRANCE from the FDA. IBRANCE is the first CDK 4/6 inhibitor approved in the United States.

APRIL: Pfizer announces that PALOMA-3 met its primary endpoint of demonstrating an improvement in PFS. The study was stopped early due to efficacy based on an assessment by an independent Data Monitoring Committee (DMC).

MAY: Pfizer presents detailed results from PALOMA-3 at the Annual Meeting of the American Society of Clinical Oncology (ASCO) in Chicago. Results are simultaneously published in *The New England Journal of Medicine.*[9]

AUGUST: The European Medicines Agency (EMA) validates for review the Marketing Authorization Application (MAA) for IBRANCE in combination with endocrine therapy for the treatment of HR+/HER2- advanced or metastatic breast cancer.

AUGUST: The Phase 3 PALLAS trial evaluating IBRANCE in pre- and postmenopausal women or men with Stage 2 or 3 HR+/HER2- early breast cancer is initiated, led by the Alliance Foundation Trials, LLC (AFT) and the Austrian Breast & Colorectal Cancer Study Group (ABCSG).

DECEMBER: Pfizer announces that its supplemental New Drug Application to expand the approved use of IBRANCE, based on data from the PALOMA-3 trial, has been accepted for filing and granted Priority Review by the FDA.

2016

FEBRUARY: The FDA approves a second indication expanding the use of IBRANCE for the treatment of HR+/HER2- advanced or metastatic breast cancer in combination with fulvestrant in women with disease progression following endocrine therapy.[1]

APRIL: Pfizer announces positive top-line results from PALOMA-2, which demonstrate IBRANCE plus letrozole prolonged PFS compared to placebo plus letrozole.

JUNE: Detailed PALOMA-2 results are presented at ASCO.

SEPTEMBER: The Committee for Medicinal Products for Human Use (CHMP) of the EMA adopts a positive opinion recommending that IBRANCE be granted marketing authorization in the European Union.

OCTOBER: IBRANCE recognized for innovation in pharmaceutical research at the 10th Annual Prix Galien USA Awards.

NOVEMBER: The EC approved IBRANCE for the treatment of women with HR+/HER2- locally advanced or metastatic breast cancer. The approval is for IBRANCE to be used in combination with an aromatase inhibitor. The approval also covers the use of IBRANCE in combination with fulvestrant in women who have received prior endocrine therapy.[17] Results from PALOMA-2 are published in *The New England Journal of Medicine.*[7]

2017

MARCH: The FDA approves a supplemental New Drug Application for IBRANCE, based on the results from PALOMA-2, converting the accelerated approval of IBRANCE to regular approval and broadening the range of anti-hormonal therapy that may be administered with IBRANCE. IBRANCE now is indicated in combination with an aromatase inhibitor, expanding on its earlier indication with letrozole, as initial endocrine based therapy for postmenopausal women with HR+/HER2- advanced or metastatic breast cancer.[1]

METASTATIC BREAST CANCER:

THE UNFAMILIAR STAGE OF A WELL-KNOWN DISEASE

BREAST CANCER IS THE MOST COMMON CANCER IN WOMEN WITH NEARLY
1.7 MILLION NEW CASES DIAGNOSED EACH YEAR WORLDWIDE[1]

5-10% OF WOMEN
PRESENT WITH PRIMARY METASTATIC DISEASE AT INITIAL DIAGNOSIS[2]

WHILE THE MAJORITY OF WOMEN ARE DIAGNOSED EARLY, THE RISK OF **METASTASIS REMAINS**

IN DEVELOPED COUNTRIES,
UP TO 30%
OF WOMEN DIAGNOSED WITH EARLIER STAGES OF BREAST CANCER PROGRESS TO METASTATIC DISEASE[3,4]

So advanced, it not only cleans and disinfects – it flies.

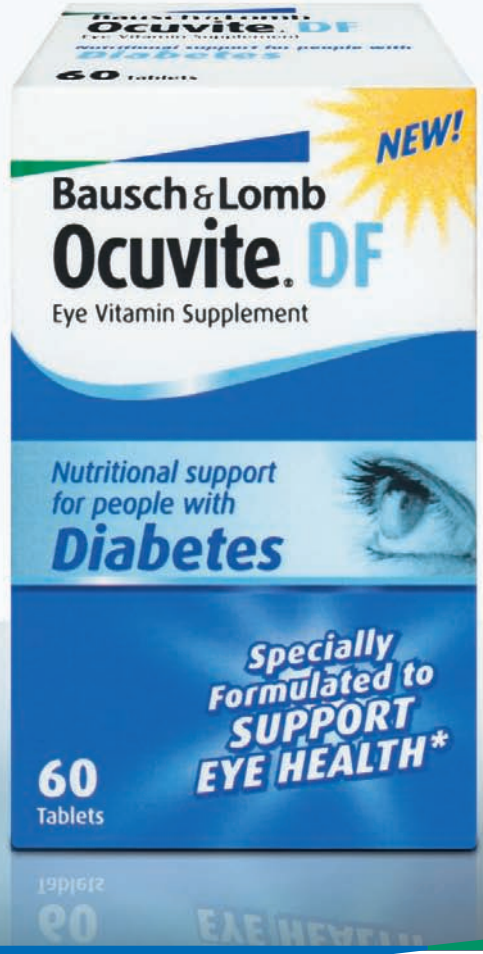
New Bausch & Lomb lens solutions — now in airport-friendly sizes.

Introducing Bausch & Lomb ReNu® and Bausch & Lomb Boston® Travel Kits. These multi-purpose solutions are not only clinically proven to kill germs and keep eyes comfortable, they're also made to meet the TSA 3 oz. carry-on limit. Clearly, the only way to fly.

For more travel tips, visit bausch.com

Bausch & Lomb
Perfecting Vision. Enhancing Life.®

Now people with diabetes have an option for the nutritional support their eyes need.



Introducing Bausch & Lomb Ocuvite® DF Eye Vitamin Supplements.

A major risk for people with diabetes is an increased chance for vision loss. High blood glucose levels increase oxidative stress, which damages the retina over time.

That's why Bausch & Lomb developed Ocuvite DF Eye Vitamin Supplements. Ocuvite DF contains the antioxidant Genistein. In combination with other essential nutrients, Genistein may help fight oxidative stress.*

To help maintain your eye health, it may help to start taking Ocuvite DF now.

***These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure or prevent any disease.**

Bausch & Lomb
Perfecting Vision. Enhancing Life.®

Now, a cereal designed to spike your taste buds, not your blood sugar.

Introducing delicious Glucerna® Cereals.

Put some crunch back in your day with three irresistible cereals, all made with our unique carbohydrate blend clinically shown to help manage your blood sugar spikes.

Look for Glucerna Cereals near the pharmacy section of your local retail store.

Glucerna. Smart nutrition for people with diabetes.™

Visit Glucerna.com for your coupon and to learn more.

Use Glucerna under medical supervision as part of your diabetes management plan.

A new and improved recipe.
A new go-anywhere bottle.
Now you're on your way to helping control diabetes.

Delicious Glucerna® Shakes offer more help with diabetes management than ever:

- A new, unique carb blend clinically shown to help manage your blood sugar.
- Chromium Picolinate to help your body's own insulin work better.
- Plant-based Omega-3s to help support circulatory and heart health.*

And Glucerna's creamy, rich shakes are so delicious, they've won the ChefsBest™ Award for Best Taste.**

Glucerna. Smart nutrition for people with diabetes.™

Visit Glucerna.com for your coupon and to learn more.

Use Glucerna under medical supervision as part of your diabetes management plan.
*400mg Omega-3 fatty acid ALA per serving (25% of 1.6g DV).
**The ChefsBest™ Award for Best Taste is awarded to the brand rated highest overall among leading brands by independent professional chefs.


lifebeyondthebathroom.com


YOU AGAIN?
lifebeyondthebathroom.com

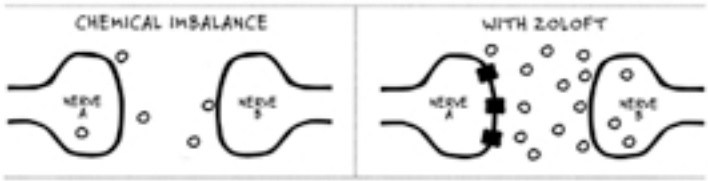
You know when you feel the weight of sadness.

You may feel exhausted, hopeless, and anxious.

Whatever you do, you feel lonely and don't enjoy the things you once loved.

Things just don't feel like they used to.

These are some symptoms of depression. They must last each day for at least two weeks and interfere with your daily life. Depression is a serious medical condition. It affects over 20 million Americans. While the cause is not known, depression may be related to an imbalance of natural chemicals between nerve cells in the brain.



Prescription ZOLOFT works to correct this imbalance.

Only your doctor can diagnose depression. ZOLOFT is not for everyone. It is approved for adults 18 and over. People taking MAOIs or pimozide shouldn't take ZOLOFT. Side effects may include dry mouth, insomnia, sexual side effects, diarrhea, nausea, and sleepiness. Please see the following page for additional information about ZOLOFT 25mg, 50mg, and 100mg tablets.

Talk to your doctor about ZOLOFT, the #1 prescribed brand of its kind.

Call 1-800-6-ZOLOFT or visit www.ZOLOFT.com for more information.

zoloft®
(sertraline HCl)

When you know more about what's wrong, you can help make it right.™

Does your allergy medicine treat both indoor and outdoor allergies?

If not, ask your doctor about switching to Zyrtec.

To learn more, visit www.zyrtec.com or call 1-800-ZYRTEC-2.

Unlike some allergy medicines, prescription Zyrtec® is approved to treat all your indoor and outdoor allergies. Like grass. Ragweed. Dust. Mold. And even pet dander.

In fact, no other antihistamine is approved to treat more allergies than Zyrtec. And if you're currently taking Zyrtec, remember to ask your doctor for a refill on your prescription.

The most common side effect was feeling drowsy. Some of the others were feeling tired and dry mouth. Most were mild to moderate.

ZYRTEC®
cetirizine HCl

Lots of allergies. Just one Zyrtec.™

(Zur'-tek)

Please see important information about Zyrtec 5-mg and 10-mg tablets and 1-mg/mL syrup on the next page.