



# New Data at ASH 2014 Highlight Progress of Pfizer's Growing Portfolio in Blood Cancers

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MYLOTARG™ (gemtuzumab ozogamicin) Demonstrates Promising Efficacy Across Multiple Phase 3 Studies in First-Line Acute Myeloid Leukemia (AML)<sup>1,2</sup> Pfizer in Discussions with Regulators on Path Forward for MYLOTARG New Long-Term, Follow-Up Data Show Chronic Myeloid Leukemia (CML) Patients Benefit from BOSULIF® (bosutinib) at 4 and 5 years<sup>3,4</sup> Inotuzumab Ozogamicin Shows Activity in Phase 2 Study of Relapsed/Refractory (R/R) Acute Lymphoblastic Leukemia (ALL)<sup>5</sup>

Pfizer Inc. (NYSE:PFE) today announced the presentation of encouraging early- and late-stage data from clinical studies across several hematologic malignancies, including acute myeloid leukemia (AML), acute lymphoblastic leukemia (ALL) and chronic myeloid leukemia (CML). Among the highlights are results from several investigator-led, large, randomized studies evaluating the antibody-drug conjugate (ADC) MYLOTARG (gemtuzumab ozogamicin) in select adult AML populations. Research was presented at the 56th Annual Meeting of the American Society of Hematology (ASH) in San Francisco, December 6-9.

“It is gratifying to see continued progress of Pfizer’s in-line and pipeline portfolio against a broad array of hematologic malignancies,” said Mace Rothenberg, senior vice president of Clinical Development and Medical Affairs and chief medical officer for Pfizer Oncology. “In particular, we are encouraged by the significant clinical evidence emerging from large randomized trials, such as AML-19 and ALFA-0701, demonstrating a positive impact of MYLOTARG when added to standard first-line treatment for patients with acute myeloid leukemia. We are engaging in discussions with the U.S. Food and Drug Administration (FDA) and other health authorities to determine the best path forward for MYLOTARG. In addition, we plan to initiate an expanded access protocol for the therapy by the end of

2014 in the United States in patients with relapsed or refractory acute myeloid leukemia for whom there are no other treatment options.”

#### MYLOTARG™ (gemtuzumab ozogamicin)

Oral and poster presentations focused on the efficacy of MYLOTARG in previously untreated patients with AML. Two oral presentations included:

AML-19 (abstract #619): This investigator-led, randomized, Phase 3 study (N=237) found that MYLOTARG significantly improved overall survival (OS) in elderly patients with AML not considered fit for intensive chemotherapy, compared to best supportive care (BSC) (median 4.9 versus 3.6 months; HR: 0.69; 95 percent CI: 0.53-0.90; P=0.005). The most common grade  $\geq 3$  adverse events (AEs) for MYLOTARG versus BSC included infection (35.1 versus 34.3 percent), febrile neutropenia (18 versus 23.7 percent), bleeding (12.6 versus 12.3 percent), fatigue (11.7 versus 21 percent) and cardiac toxicity (6.3 versus 14 percent). The study was conducted by the European Organization for the Research and Treatment of Cancer (EORTC) and Gruppo Italiano Malattie Ematologiche dell'Adulto (GIMEMA) leukemia groups.<sup>1</sup> ALFA-0701 (abstract #376): This investigator-led, randomized, Phase 3 study (N=278) demonstrated a combination of MYLOTARG and a standard-of-care chemotherapy regimen (daunorubicin and cytarabine) significantly improved event-free survival (EFS) and relapse-free survival (RFS) in adult AML patients at three years, compared to induction chemotherapy alone (EFS: 31 percent versus 19 percent; HR=0.66; 95 percent CI: 0.50-0.87; median 9.7 versus 15.6 months; P=0.0026) (RFS: 38 percent versus 25 percent; P=0.006). In terms of safety, MYLOTARG patients were more likely to experience persistent thrombocytopenia (15 percent) as well as two or more serious adverse events (SAEs)(P=0.031). The study was conducted by the Acute Leukemia French Association (ALFA) in collaboration with Pfizer.<sup>2</sup>

More information on AML-19, ALFA-0701 and other abstracts evaluating MYLOTARG can be found on the ASH website.

#### BOSULIF® (bosutinib)

Pfizer presented long-term follow-up data from the Pfizer-sponsored pivotal study of BOSULIF in patients with refractory CML. These analyses demonstrated durable clinical benefit in multiple treatment settings. At five years (publication-only abstract), 41 percent of patients with chronic phase (CP) CML in the second-line setting (n=284) remained on treatment, and importantly, at four years (abstract #4559), 24 percent of patients receiving BOSULIF as third-line therapy (n=119) remained on treatment.<sup>3,4</sup>

Treatment emergent adverse events (TEAEs) in the five- and four-year data were consistent with the known safety profile of BOSULIF.<sup>3,4</sup> In the five-year analysis, the most common grade 3 and/or 4 TEAEs for second-line CP CML patients included diarrhea (10 percent), nausea (1 percent), vomiting (4 percent), rash (9 percent) and thrombocytopenia (26 percent).<sup>4</sup> In the four-year analysis, the most common grade 3 and/or 4 TEAEs for third-line CP CML patients included diarrhea (9 percent), nausea (1 percent), vomiting (1 percent), rash (3 percent), headache (3 percent), abdominal pain (1 percent), fatigue (2 percent), thrombocytopenia (26 percent), neutropenia (16 percent) and anemia (7 percent).<sup>3</sup>

### Inotuzumab Ozogamicin

New Pfizer-sponsored data also included a Phase 2 study (N=35) (abstract #2255) of inotuzumab ozogamicin, an investigational CD22-directed ADC, demonstrating clinical activity in relapsed/refractory (R/R) adult ALL patients. The majority of patients (69 percent; 95 percent CI: 50.7-83.2) achieved a complete response (CR) or CR without complete neutrophil count or platelet recovery (CRi). In addition, 75 percent of CR+CRi patients achieved minimal residual disease (MRD) negativity, an indicator of remission. Common grade  $\geq 3$  AEs included thrombocytopenia (34 percent), neutropenia (20 percent) and febrile neutropenia (20 percent).<sup>5</sup> The randomized, Phase 3 INO-VATE ALL trial is ongoing in a similar patient population, with top-line results expected in 2015.<sup>6</sup>

Additionally, an investigator-led Phase 1/2 study (abstract #794) demonstrated that inotuzumab ozogamicin added to low intensity chemotherapy (cyclophosphamide, dexamethasone, methotrexate and cytarabine) had clinical activity in previously untreated older patients ( $\geq 60$  years) with ALL. In the study, 96 percent of evaluable patients (N=26) achieved CR or CR without complete platelet recovery (CRp) at the 13-month follow-up. All patients who achieved CR+CRp also achieved MRD negativity. Grade 3 and/or 4 toxicities included infections (85 percent), prolonged thrombocytopenia (65 percent), hyperglycemia (44 percent), increased bilirubin (22 percent), intracranial hemorrhage (15 percent), increased amino alanine transferase (ALT) (11 percent), hematuria (7 percent), headache (4 percent), cognitive disturbance (4 percent), ascites (4 percent) and diarrhea (4 percent). The study was conducted by The University of Texas MD Anderson Cancer Center.<sup>7</sup>

### ABOUT BOSULIF® (bosutinib)

BOSULIF® (bosutinib) is an oral, once-daily, tyrosine kinase inhibitor (TKI), which inhibits the Bcr-Abl kinase that promotes CML; it is also an inhibitor of Src-family kinases.

BOSULIF® is currently approved in the U.S. for the treatment of adult patients with Philadelphia chromosome-positive (Ph+) CML with resistance or intolerance to prior therapy and offers an important treatment option for these patients. In Europe, BOSULIF was granted conditional marketing authorization for the treatment of adult patients with Ph+ CML previously treated with one or more TKIs and for whom imatinib, nilotinib and dasatinib are not considered appropriate treatment options. The current approved dose of BOSULIF® is 500 mg orally once daily with food.

The potential of BOSULIF® in previously untreated patients with CML at a 400 mg dose is being investigated in the ongoing Phase 3 BFORE trial as part of a novel, co-development partnership between Pfizer and Avillion LLP.<sup>8</sup>

#### IMPORTANT BOSULIF® (bosutinib) SAFETY INFORMATION

**Contraindication:** Hypersensitivity to BOSULIF. Anaphylactic shock occurred in less than 0.2% of treated patients.

**Gastrointestinal Toxicity:** Diarrhea, nausea, vomiting, and abdominal pain can occur. In the clinical trial, median time to onset for diarrhea was 2 days, median duration was 1 day, and median number of episodes per patient was 3 (range 1-221). Monitor and manage patients using standards of care, including antidiarrheals, antiemetics, and/or fluid replacement. Withhold, dose reduce, or discontinue BOSULIF as necessary.

**Myelosuppression:** Thrombocytopenia, anemia, and neutropenia can occur. A complete blood count should be performed weekly for the first month and then monthly or as clinically indicated. Withhold, dose reduce, or discontinue BOSULIF as necessary.

**Hepatic Toxicity:** Twenty percent of patients experienced an increase in either ALT or AST. Liver enzyme elevation usually occurs early in treatment. Perform monthly hepatic enzyme tests for the first 3 months and as clinically indicated. In patients with transaminase elevations, monitor liver enzymes more frequently. Drug-induced liver injury has occurred. Withhold, dose reduce, or discontinue BOSULIF as necessary.

**Fluid Retention:** Fluid retention can occur and may cause pericardial effusion, pleural effusion, pulmonary edema, and/or peripheral edema. Monitor and manage patients using standards of care. Interrupt, dose reduce, or discontinue BOSULIF as necessary.

**Embryofetal Toxicity:** BOSULIF may cause fetal harm when administered to a pregnant woman. Women of childbearing potential should be advised of potential hazard to the fetus and to avoid becoming pregnant while receiving BOSULIF.

**Adverse Reactions:** The most common adverse reactions observed in greater than 20% of patients in the Phase 1/2 safety population (N=546) were diarrhea, nausea, thrombocytopenia, vomiting, abdominal pain, rash, anemia, pyrexia, and fatigue.

The most common Grade 3/4 adverse reactions and laboratory abnormalities observed in greater than 10% of patients were thrombocytopenia, anemia, and neutropenia.

**Hepatic Impairment:** In patients with pre-existing mild, moderate, and severe hepatic impairment, the recommended dose of BOSULIF is 200 mg daily.

**Renal Impairment:** For patients with pre-existing severe renal impairment (CrCL less than 30 mL/min), the recommended BOSULIF dose is 300 mg daily.

**CYP3A Inhibitors and Inducers:** Avoid concurrent use with strong or moderate CYP3A inhibitors or inducers.

**Proton Pump Inhibitors:** Consider using short-acting antacids or H2 blockers instead of PPIs. Separate antacid or H2 blocker dosing and BOSULIF dosing by more than 2 hours.

**Substrates of P-glycoprotein:** BOSULIF may increase the plasma concentrations of drugs that are P-gp substrates, such as digoxin.

**Nursing Mothers:** Given the potential for serious adverse reactions in nursing infants, a decision should be made whether to discontinue nursing or BOSULIF.

Please see full Prescribing Information at [www.bosulif.com](http://www.bosulif.com).

## ABOUT PFIZER ONCOLOGY

Pfizer Oncology is committed to the discovery, investigation and development of innovative treatment options to improve the outlook for cancer patients worldwide. Our strong pipeline of biologics and small molecules, one of the most robust in the industry, is studied with precise focus on identifying and translating the best scientific breakthroughs into clinical application for patients across a wide range of cancers. By working collaboratively with academic institutions, individual researchers, cooperative research groups, governments, and licensing partners, Pfizer Oncology strives to cure or control cancer with breakthrough medicines, to deliver the right drug for each patient at the right time. For more information, please visit [www.Pfizer.com](http://www.Pfizer.com).

PFIZER INC.: WORKING TOGETHER FOR A HEALTHIER WORLD®

At Pfizer, we apply science and our global resources to bring therapies to people that extend and significantly improve their lives. We strive to set the standard for quality, safety and value in the discovery, development and manufacture of health care products. Our global portfolio includes medicines and vaccines as well as many of the world's best-known consumer health care products. Every day, Pfizer colleagues work across developed and emerging markets to advance wellness, prevention, treatments and cures that challenge the most feared diseases of our time. Consistent with our responsibility as one of the world's premier innovative biopharmaceutical companies, we collaborate with health care providers, governments and local communities to support and expand access to reliable, affordable health care around the world. For more than 150 years, Pfizer has worked to make a difference for all who rely on us. To learn more, please visit us at [www.pfizer.com](http://www.pfizer.com).

### About the EORTC

The European Organisation for the Research and Treatment of Cancer (EORTC) brings together European cancer clinical research experts from all disciplines for trans-national collaboration.

Both multinational and multidisciplinary, the EORTC Network comprises more than 2,500 collaborators from all disciplines involved in cancer treatment and research in more than 300 hospitals in over 30 countries.

Through translational and clinical research, the EORTC offers an integrated approach to drug development, drug evaluation programs and medical practices.

EORTC Headquarters, a unique pan European independent clinical research infrastructure, is based in Brussels, Belgium, from where its various activities are coordinated and run. [www.eortc.org](http://www.eortc.org)

DISCLOSURE NOTICE: The information contained in this release is as of December 9, 2014. Pfizer assumes no obligation to update forward-looking statements contained in this release as the result of new information or future events or developments.

This release contains forward-looking statements about Mylotarg, Bosulif and Inotuzumab Ozogamicin that involve substantial risks and uncertainties that could cause actual results to differ materially from those expressed or implied by such statements. Forward-looking statements include statements regarding the potential benefits of such products and product candidates, as well as clinical trial data relating to such products and product candidates and the potential implications of such data. Risks and uncertainties include,

among other things, the uncertainties inherent in research and development, including the possibility of unfavorable clinical trial results, including unfavorable new clinical data and additional analyses of existing clinical data; uncertainties regarding the outcome of our discussions with the FDA and other regulatory authorities regarding the path forward for Mylotarg; whether and when new drug applications or supplemental drug applications may be filed in any jurisdictions for any of such products and product candidates; whether and when regulatory authorities will approve any such applications as well as their decisions regarding labeling and other matters that could affect the availability or commercial potential of such products and product candidates; and competitive developments.

A further description of risks and uncertainties can be found in Pfizer's Annual Report on Form 10-K for the fiscal year ended December 31, 2013 and in its subsequent reports on Form 10-Q, including in the sections thereof captioned "Risk Factors" and "Forward-Looking Information That May Affect Future Results", as well as in its subsequent reports on Form 8-K, all of which are filed with the SEC and available at [www.sec.gov](http://www.sec.gov) and [www.pfizer.com](http://www.pfizer.com).

1 ASH Accepted Abstract #619 Improved Overall Survival with Gemtuzumab Ozogamicin (GO) Compared with Best Supportive Care (BSC) in Elderly Patients with Untreated Acute Myeloid Leukemia (AML) Not Considered Fit for Intensive Chemotherapy: Final Results From The Randomized Phase III study (AML-19) of The EORTC and GIMEMA Leukemia Groups. Oral Presentation, December 8, 2014: 7:30pm ET. S Amadori – Presenter. 56th American Society of Hematology Annual Meeting. San Francisco, CA. December 6-9, 2014. 2 ASH Accepted Abstract #376 Final Analysis of the ALFA 0701 Study. Oral Presentation, December 8, 2014: 2:00pm ET. S Castaigne – Presenter. 56th American Society of Hematology Annual Meeting. San Francisco, CA. December 6-9, 2014. 3 ASH Accepted Abstract #4559 Bosutinib As Third-Line Therapy in Patients (Pts) with Chronic Phase Chronic Myeloid Leukemia (CP CML) Following Failure with Imatinib Plus Dasatinib and/or Nilotinib: 48-Month Update of a Phase 1/2 Study. Poster Presentation, December 8, 2014: 9:00-11:00pm ET. C Gambacorti-Passerini – Presenter. 56th American Society of Hematology Annual Meeting. San Francisco, CA. December 6-9, 2014. 4 ASH Accepted Abstract Bosutinib As Second-Line Therapy in Patients (Pts) With Chronic Phase Chronic Myeloid Leukemia (CP CML) Resistant or Intolerant to Prior Imatinib: 60-Month Update of a Phase 1/2 Study. Publication Only. 56th American Society of Hematology Annual Meeting. San Francisco, CA. December 6-9, 2014. 5 ASH Accepted Abstract #2255 A Phase II Study of Weekly Inotuzumab Ozogamicin (InO) in Adult Patients with CD22-Positive Acute Lymphoblastic Leukemia (ALL) in Second or Later Salvage. Poster Presentation, December 7, 2014: 9:00-11:00pm ET. A Advani – Presenter. 56th American

Society of Hematology Annual Meeting. San Francisco, CA. December 6-9, 2014.

6 Clinicaltrials.gov. A Study Of Inotuzumab Ozogamicin Versus Investigator's Choice Of Chemotherapy In Patients With Relapsed Or Refractory Acute Lymphoblastic Leukemia. Available

at: <http://clinicaltrials.gov/ct2/show/NCT01564784?term=inotuzumab+ozogamicin&spons=Pfizer>

Accessed on: December 5, 2014. 7 ASH Accepted Abstract #794 Inotuzumab Ozogamicin in Combination with Low-Intensity Chemotherapy (mini-hyper-CVD) As Frontline Therapy for Older Patients ( $\geq 60$  years) with Acute Lymphoblastic Leukemia (ALL). Oral Presentation, December 9, 2014: 10:45am ET. E Jabbour – Presenter. 56th American Society of Hematology Annual Meeting. San Francisco, CA. December 6-9, 2014.

8 Clinicaltrials.gov. A Multicenter Phase 3, Open-Label Study of Bosutinib Versus Imatinib in Adult Patients With Newly Diagnosed Chronic Phase Chronic Myelogenous Leukemia. Available

at: <http://clinicaltrials.gov/ct2/show/NCT02130557?term=NCT02130557&rank=1>.

Accessed on: December 5, 2014.

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