



To Our Shareholders

## In 2008, OSI Achieved Sustained Profitability

OSI EX. 2014 - 0002

Tarceva Worldwide Sales	\$1.12 billion
Total Revenues	\$379 million
Pre-Tax Income from Continuing Operations	\$133 million
Net Income from Continuing Operations	\$467 million
Ending 2008 Cash	\$516 million

In order to provide additional, meaningful comparisons for our 2008 results, we provided the following adjusted, or non-GAAP, financial measures during our 2008 year-end earnings call:

In millions, except per share amounts

	<u>Net Income</u> <u>from</u> <u>continuing</u> <u>operations</u>	<u>Fully</u> <u>Diluted</u> <u>EPS</u>
<b>2008 GAAP Results</b>	\$467	\$7.34
<b><u>2008 Non-GAAP Adjustments</u></b>		
Valuation Allowance Gain	(\$337)	(\$5.20)
<b>2008 Non-GAAP Results</b>	\$130	\$2.14
<b><u>2008 Non-GAAP Pro Forma Adjustments</u></b>		
Retrospective Impact of APB 14-1	(\$13)	(\$0.12)
Imposition of 2009 Statutory Tax Rate	(\$44)	(\$0.78)
<b>2008 Non-GAAP Pro Forma</b>	\$73	\$1.24

Weighted Average Diluted Shares Outstanding

<b>2008 GAAP Results</b>	66.9
<b>2008 Non-GAAP<sup>1</sup></b>	64.3
<b>2008 Pro Forma<sup>1</sup></b>	60.4

<sup>1</sup> The decrease in weighted shares outstanding is due to lower adjusted net income.

### *Use of Non-GAAP Financial Measures*

The table above presents both generally accepted accounting principles (GAAP) and non-GAAP financial measures for the year ended December 31, 2008. The non-GAAP financial measures include adjusted net income from continuing operations and adjusted earnings per share from continuing operations, each of which has a GAAP equivalent. We have provided these non-GAAP financial measures to adjust for the impact of a \$337 million non-cash gain in the fourth quarter of 2008 related primarily to our expected utilization of net operating loss carryforwards. These non-GAAP financial measures also include certain proforma adjustments, which assume that the following items were in effect for the fiscal year ended December 31, 2008: (i) the adoption of FASB Staff Position APB 14-1 which required us to recognize additional non-cash interest expense related to our convertible debt instruments beginning in 2009; and (ii) the increase in our income tax expense to a 40% effective rate, even though we expect to continue to pay cash taxes at 2% to 4% alternative minimum tax rates. We believe that the non-GAAP financial measures included above provide investors with (i) financial measures that we use in the management of our business and (ii) additional, meaningful comparisons of current results to prior periods' results by excluding the impact of significant non-cash items that we do not believe reflect our fundamental business performance. These non-GAAP measures should not be considered in isolation of, or

2008 was another year of real scientific progress and strong financial performance for our company. In November, Tarceva® crossed the \$1 billion annual sales mark – achieving this universally recognized metric for a “Blockbuster” medicine within four years of launch – and finished the year with annual global sales of \$1.12 billion, up 27% on 2007 sales. OSI corporate revenues of \$379 million fueled adjusted net income from continuing operations of \$130 million (up 26% from the prior year) and adjusted earnings per share from continuing operations of \$2.14, up from \$1.70 in 2007 (see accompanying chart on preceding page for reconciliation of all adjusted measures). Balance sheet “cash and short-term investments” ended 2008 at approximately \$516 million and have been conservatively managed throughout the ongoing financial crisis in the global economy. We have continued to manage our cost base judiciously and the emergence of significant DP-IV patent estate revenues – which contributed over 10% of 2008 revenues – has added important diversity to our revenue line. We expect this to be a major contributor to our revenue growth rate going forward as this class of diabetes drugs continues to expand in use.

We strive for an effective balance between financial performance and

the ability to re-invest in our mission of developing innovative and differentiated new medicines that deliver meaningful strides forward in the treatment of cancer and diabetes/obesity for patients around the world. In 2008, we invested approximately \$139 million in a research and development program that:

- (i) Yielded a major Phase III success for Tarceva in the SATURN trial (potentially allowing the expansion of its use to earlier stage lung cancer patients – a position reinforced by the subsequent success of the ATLAS trial in early 2009);
- (ii) Saw the continued expansion of our R&D efforts to explore Tarceva use beyond its core indications in second-/third-line non-small cell lung cancer (NSCLC) and first-line pancreatic cancer;
- (iii) Included the advancement of all four of our primary development candidates (OSI-906, OSI-027, PSN821 & PSN602) in clinical trials (creating a *bona fide* clinical pipeline of wholly owned assets arising from our internal *de novo* drug discovery research); and
- (iv) Continued to establish our research groups as recognized leaders in the areas of epithelial-to-mesenchymal transition (EMT) biology in cancer and in the

neuroendocrine control of body weight and glycemia in the diabetes/obesity arena.

None-the-less, all this progress has occurred against the back-drop of an unprecedented global economic downturn precipitated by the banking crisis at the end of 2008. Even within this bleak overall environment, the pharmaceutical and biotechnology industries are widely perceived to be in their own acute form of turmoil. The specter of uncertainty surrounding U.S. healthcare reform (and associated pricing and reimbursement pressures); widespread pending patent expirations and poor R&D productivity in the pharmaceutical sector; a financing crisis in the biotechnology sector (which could see widespread bankruptcies for the first time in the industry’s history); increasing and profligate generic industry challenge to essentially all valuable innovator intellectual property; and intense competition in new product development, has led to widespread pessimism and anxiety amongst industry analysts and commentators alike.

And yet, despite the fact that many of these macro developments impact our business to varying degrees, we enter 2009 with a sense of growing confidence in an organization that is anchored around a proven and

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entrenched principal asset in Tarceva; possesses a high quality emerging clinical and pre-clinical pipeline; and has a solid financial strength that remains a rarity in the biotechnology sector – providing the company with appreciable strategic flexibility at a time when many biotech companies are in survival mode. The following commentary summarizes our progress as a business in 2008 and into the early part of 2009:

## TARCEVA

Tarceva is commercialized in collaboration with Roche. We receive a 50% profit share on U.S. sales of Tarceva and a 21% royalty on sales in the rest of the world. Tarceva's significant global growth in 2008 was driven primarily by ex-U.S. sales which increased by nearly \$200 million from \$470 million in 2007 to \$665 million in 2008. The first full year of sales in the Japanese market was an important part of this growth. In addition, Tarceva was endorsed in November by the UK's National Institute for Health and Clinical Excellence (NICE) as an alternative treatment to the intravenous chemotherapy agent docetaxel for the second-line treatment of advanced NSCLC. Lung cancer patients in England, Wales and Northern Ireland will now have access to an oral targeted therapy

that has been approved throughout Europe for advanced NSCLC. Tarceva has received regulatory approval in a total of 94 countries for NSCLC and 70 countries for pancreatic cancer.

The more modest growth seen in the U.S. market (2008 sales of \$457 million versus 2007 sales of \$417 million) represents a credible achievement in the face of the continuing reimbursement imbalance between older cytotoxic (and newer biological) anti-cancer drugs reimbursed under the Medicare Part B regulations and the new generation of oral anti-cancer medicines like Tarceva, Gleevec®, Sutent® and Nexavar® which are reimbursed under the newer Part D regulations. Patients receiving oral medicines have higher effective co-payments and co-insurance obligations to meet – despite the fact that these oral drugs are more convenient to the patient and are often substantially cheaper than the competing cytotoxic and biological agents that are administered at the doctor's office by intravenous injection or infusion. This co-payment and co-insurance imbalance presents an even greater challenge in tough economic times when patients and their families struggle to make ends meet. We are proud of our U.S. partner Genentech's 'Access Solutions' and 'Access to Care Foundation' programs. They are

among the best in the industry and seek to provide access to Tarceva patients who can't afford their medicine. However, despite the fact that market analysis throughout 2008 and into early 2009 has shown that Tarceva has held its own in market share (and even grown share in certain settings), sales have inevitably been impacted by the downturn as a greater number of patients who have been prescribed Tarceva are failing to have their prescriptions filled – most likely due to the patients' inability to afford the co-payments and co-insurance.

We were pleased to announce in November 2008 that the large, randomized, placebo-controlled Phase III study, SATURN, met its primary endpoints and showed Tarceva extended the time patients with advanced NSCLC lived without their cancer getting worse when Tarceva is given immediately following initial treatment with platinum-based chemotherapy (as defined by progression-free survival). We believe that Tarceva, as a once-a-day oral therapy, is well suited for first-line maintenance treatment for patients with advanced NSCLC. The data will be formally presented to the medical community at the Annual Meeting of the American Society of Clinical Oncology (ASCO) in Orlando, May 29 – June 2, 2009. Overall survival was one of the sec-



In 2008 Tarceva global sales exceeded \$1 billion, achieving “Blockbuster” status within 4 years of launch.

Tarceva is approved in 94 countries for NSCLC

ondary endpoints and we anticipate mature survival data in the second half of 2009.

In March 2009, our regulatory team submitted a supplemental New Drug Application (sNDA) for the use of Tarceva as a first-line maintenance therapy in the treatment of NSCLC patients. Simultaneously, Roche filed an application in Europe with the European Medicines Agency (EMA). Assuming acceptance of the U.S. filing, we would expect a PDUFA date in or about mid-January 2010 and, if Tarceva is successfully registered, we would anticipate approval and launch in the first quarter of 2010.

Clinical data supporting the use of Tarceva in the NSCLC maintenance setting was enhanced in early 2009 when our partner Roche announced that a Phase III study, ATLAS, conducted by their U.S. Genentech organization was stopped early on the recommendation of an independent data safety monitoring board. A pre-planned interim analysis showed that combining Tarceva and Avastin® significantly extended the time NSCLC patients lived without their cancer getting worse, as defined by progression-free survival, compared with Avastin plus placebo following initial treatment with platinum-based chemotherapy and Avastin. In both

these key SATURN and ATLAS studies preliminary safety analyses showed adverse events were consistent with previous Tarceva studies as well as trials evaluating Tarceva and Avastin together, and no new safety signals were observed.

Unfortunately, a third major Phase III trial, The BeTa-Lung study, in which Tarceva and Avastin were compared to Tarceva and placebo in second-line NSCLC patients failed to meet its primary endpoint of overall survival. The BeTa study was noteworthy in that this was the first prospective, randomized study in which Tarceva was dosed to only a second-line NSCLC patient population, and the data in the Tarceva-only arm (which had a median survival of 9.2 months) were consistent with the earlier second-line subset findings from the pivotal second-/third-line NSCLC study, BR.21.

On a more positive note, our clinical and regulatory teams were successful in executing a clinical program and regulatory process that resulted in an important label update on Tarceva dose modification in those NSCLC patients who continue to smoke. The Tarceva label now states that "Cigarette smoking has been shown to reduce erlotinib exposure" and that a "cautious increase in the dose

of Tarceva, not exceeding 300mg" can be considered by physicians treating lung cancer patients who continue to smoke. Although the efficacy and long-term safety of a higher dose has not been established in a prospective trial for patients who continue to smoke, the update provides physicians with important information as they consider treatment options for this group of patients.

We continue to invest in a substantial ongoing life cycle plan for Tarceva which seeks to expand Tarceva use to the adjuvant setting in NSCLC (through an OSI conducted Phase III study known as RADIANT which is expected to complete enrollment in 2010) and to new disease indications like ovarian cancer (where an EORTC front-line maintenance Phase III study is expected to read-out top-line data in 2010) and hepatocellular carcinoma (where a collaborative Phase III study with Bayer/Onyx investigating the use of Tarceva in combination with Nexavar is due to start imminently). In addition, we continue to expect data from the CALGB study in "never-smoker," first-line NSCLC patients in 2009.

## TARCEVA INTELLECTUAL PROPERTY

Tarceva's success also means that it

Tarceva patient, Ann Dudurich, finishes a 30-mile fundraiser bike ride after being diagnosed with Stage IV lung cancer in January 2007. Ann shared her inspirational story battling lung cancer with OSI employees in February 2009.



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