

**(osi)** pharmaceuticals

Shaping medicine, changing lives.™

May 2007

Shareholder Letter



## To Our Shareholders

**W**e are delighted to be able to share this letter with you at a time when the Company has so recently achieved a seminal advance in our history – that of transitioning to profitability. During the first quarter of 2007 we delivered a strong \$0.33 per share earnings from our continuing operations and fully expect to maintain this momentum through 2007.



Colin Goddard, Ph.D.  
Chief Executive Officer

This achievement comes nearly ten years after our decision to systematically build away from the technology platform services model - which allowed us to lay down a strong drug discovery sciences base in the early 1990's - and just 29 months since the U.S. approval of our flagship anti-cancer therapy Tarceva®.

Over the last decade we have been focused on ensuring that we bring Tarceva to cancer patients in desperate need of innovative next-generation molecular targeted therapies while simultaneously laying the foundation from which to build an outstanding biotechnology organization around this success. We continue today to be completely committed to meeting the needs of patients and shareholders alike. We firmly believe that striving for the optimal balance between financial performance and reinvestment in the discovery, development and commercialization of innovative therapies for patients suffering from cancer, diabetes and obesity is the best way to realize significant long term shareholder value.



Robert A. Ingram  
Chairman of the Board

Transitioning from a development stage organization to a more mature and commercially sustainable company has been a challenging journey for those - still relatively few - biotechnology companies who, like us, have achieved a major product success. In preparing for, and executing upon, this transition at OSI we have achieved many milestones including:

- The successful development and registration of Tarceva which is now available in over 100 countries around the world following the demonstration of a survival benefit in Phase III trials using Tarceva in treatment regimens for advanced non-small cell lung cancer and pancreatic cancer – two of the most difficult to treat and deadly forms of cancer;
- The treatment of well over 100,000 cancer patients with Tarceva - adding an estimated 20,000 years of life to these patients - translating to \$650 million global sales in 2006 alone, just the second full year on the market in the U.S. and the first full year of sales in Europe;
- The execution of multiple successful financings and debt issuances to effectively capitalize the Company for future growth;
- The systematic addition of key development, registration and commercial assets and know-how that have allowed us to play a key role in maximizing the value of Tarceva within our global alliance for the brand with Genentech, Inc. and Roche;
- The evolution, through M&A and *de novo* investment, of a sound and differentiated R&D platform upon which to build in oncology;
- The highly successful \$35 million acquisition of the DPIV intellectual property platform and lead compound (PSN9301) from Probiodrug in 2004. A transaction that we believe can potentially yield a royalty annuity worth hundreds of millions of dollars from this major emerging class of diabetes therapies spearheaded by the 2006/2007 approvals of Merck's Januvia™ and Janumet™; and
- A compounded annual appreciation in the stock price of OSIP of over 30% since we embarked upon the strategy to build away from the technology platform services model in 1998.

This journey to profitability has not been without missteps – the most noticeable of which has been the very disappointing consequences of the 2005 Eyetech acquisition. We made this acquisition based on the strategic rationale that a second source of appreciable top-line revenues would help fuel growth and expand our ability to fund R&D through our transition to profitability. The key asset acquired in the transaction, Macugen®, is a selective anti-VEGF agent that was the first of its class approved for neovascular age-related macular degeneration. Our decision to acquire Eyetech was based upon three critical assumptions that have proven to be erroneous – that the off-label use of the more promiscuous anti-VEGF agent, Avastin®, would not gain traction due to safety concerns; that the FDA would curtail the unregulated/unapproved reformulation of the Avastin anti-cancer formulation for injection in the eye; and that Macugen would have a sustainable niche – based on a preferential safety profile – in the market following the launch of Lucentis®, another more promiscuous anti-VEGF agent. Although Macugen recorded \$107 million in sales in 2006 and we continue to believe that its safety profile will ultimately command a niche in the market place, there can be no doubt that this transaction was a significant miscue. We have recognized this and – in an industry that requires risk-taking but that also demands the aggressive management of risk – we have moved quickly to manage the situation. We have successively stripped costs out of the business (both the eye business and our expanding core operations in oncology and diabetes) and committed to divesting the eye business during the course of 2007. As a result we are reporting the financials of the Eyetech unit as discontinued operations through the completion of the divestiture.

As a result of this tactical miscue, we are more committed than ever to capitalize on the value we believe to be inherent in our core oncology and diabetes/obesity franchises and the last year has seen appreciable progress in this regard.

The competitive situation around Tarceva has improved noticeably with high profile Phase III failures for Telcyta™ in NSCLC and Avastin and Erbitux® in pancreatic cancer helping to reaffirm the value of Tarceva. We have also continued to execute on our joint label expansion clinical trials program with our colleagues at Genentech and Roche. A crucial Phase III study using Tarceva as a maintenance therapy following front-line treatment

regimens in NSCLC (the SATURN study) is enrolling on-track and we anticipate data from this study in the second half of 2008. The second-line (BETA) Avastin/Tarceva combination trial in NSCLC and maintenance study in ovarian cancer are also enrolling well. Our own clinical team has initiated a large Phase III trial (the RADIANT trial) which seeks to demonstrate the utility of Tarceva in an adjuvant setting following surgery and optional chemotherapy in stage I-IIIa NSCLC patients. In addition to this we have confirmed that the exposure levels of Tarceva in active smokers following regular dosing, 150mg/day, are approximately half those seen in non-smokers. Thus we will be seeking a dose modification to the package insert reflecting a new maximum tolerated dose of 300mg/day in this population of patients.

On the regulatory front, Tarceva was approved for use in pancreatic cancer in Europe in January of this year and we anticipate approval for NSCLC in Japan during 2007. Roche has successfully negotiated reimbursement agreements throughout Europe (with the exception of the UK's NICE organization where they are appealing a decision not to reimburse Tarceva in England and Wales) and the prospects continue to look good for expanding Tarceva use in ex-U.S. markets.

Tarceva sales in the U.S. have been stable in the latter part of 2006 and the early part of 2007. We believe that this is driven in part by active competition in the second/third line NSCLC market but that it is accentuated by changing reimbursement dynamics in the U.S. market. As a result of the Medicare reform, Part B (intravenously administered) drugs are no longer as favorably reimbursed as they have been in the past. However, we believe economic considerations remain an important factor in influencing choice of therapy in favor of Part B drugs especially in situations where the data may be perceived as equivocal. We believe this situation will adjust over time (as pressure on Part B reimbursement increases) and with the emergence of key new data such as that from the SATURN study.

We have also recently concluded an agreement with Genentech to realign our joint sales effort such that – effective April 1, 2007 – we will have, for the first time, a dedicated Tarceva sales force staffed 50:50 by OSI and Genentech sales representatives. This has a dual benefit to OSI in both increasing the proportion of total sales expenses for which we

are reimbursed and – more importantly - providing a focused sales effort in support of the brand.

Our translational research efforts on Tarceva have continued to yield valuable insights into both the optimal use of this agent and the impact of cancer biology on targeted therapies in general. We are continuing to investigate the complex and intertwined interactions between smoking, dose, rash and aberrations in EGFR-related cell signaling such as those resulting from mutations in the k-ras gene on Tarceva therapy. More comprehensively, we are exploring the role of the phenomena of epithelial-to-mesenchymal transition (or EMT: a central biological process involved in the systematic spread and progression of human cancer) on the responsiveness of tumors to Tarceva and other targeted therapies. Indeed we have focused our oncology research efforts on exploiting our growing understanding of this process in order to develop optimal combinations of targeted therapies that exploit this complex tumor biology. Two of our emerging pipeline of follow-on therapies – OSI-906, which targets the insulin-like growth factor receptor (IGF1-R) and OSI-027, which targets the TORC1/TORC2 protein complexes and is a next generation mTOR pathway targeted agent – could allow us to optimize combination therapies with Tarceva that exploit aspects of EMT biology. Our most advanced follow-on oncology product, OSI-930, is in the latter stages of a Phase I trial in cancer patients. OSI-930 is an oral, small molecule, co-inhibitor of the receptor tyrosine kinases c-kit and VEGFR and is, as such, targeted to simultaneously inhibit an important proliferative pathway in certain tumors and the process of angiogenesis.

Our U.K. based diabetes and obesity Prosidion subsidiary has thrived as a focused R&D franchise built around PSN9301 – our own DPIV inhibitor acquired as part of the Probiobdrug acquisition. PSN9301 is being developed with a view to mealtime or twice daily dosing (ultimately with metformin) and has demonstrated encouraging activity in Phase IIa trials. We believe its rapid absorption and clearance may allow for “interprandial sparing” whereby the inhibition of DPIP around major meals - where levels of the target glucose regulator GLP-1 are critical - can deliver the required efficacy without the potential side effects associated with sustained inhibition of other important DPIP substrates like Substance P. We expect to begin a Phase IIb trial program for PSN9301 during 2007.

Unlike the specialty market of oncology – where we expect to commercialize our future products directly in the U.S. – diabetes is a primary care market and our current model involves partnering our diabetes assets for commercialization. As such, and given the necessary constraints on our overall R&D spending as we strive to balance R&D reinvestment with financial performance, we chose to license our next most advanced diabetes clinical program – the glucokinase activator PSN010 – to Eli Lilly and Company in a transaction that yielded \$25 million in up-front fees, up to \$360 million in potential milestones and competitive royalties upon successful development and commercialization. Lilly will also be responsible for all ongoing development and commercialization costs which has allowed us to contain our overall R&D spend in this critical transitional year for the Company.

Putting this all together, we believe that we have the Company well poised as we complete our journey to profitability. We have adjusted aggressively to the miscue of the Eyetech transaction, continued to build on the value of the Tarceva franchise and achieved what we believe is an appropriate balance between key R&D investments for the Company’s longer term growth and disciplined cost-management allowing us to deliver credible earnings performance even as we build pipeline strength in oncology and diabetes/obesity.

We recognize the support of you, our shareholders, through this challenging time and remain confident in the near and long term prospects for success of our Company. We would also like to thank our employees and recognize their tremendous commitment to bringing new medicines and new hope to the millions of patients around the world who suffer from cancer, diabetes and obesity.

We thank you for your continued support and invite you to explore our new website.



Colin Goddard, Ph.D.  
Chief Executive Officer



Robert A. Ingram  
Chairman of the Board