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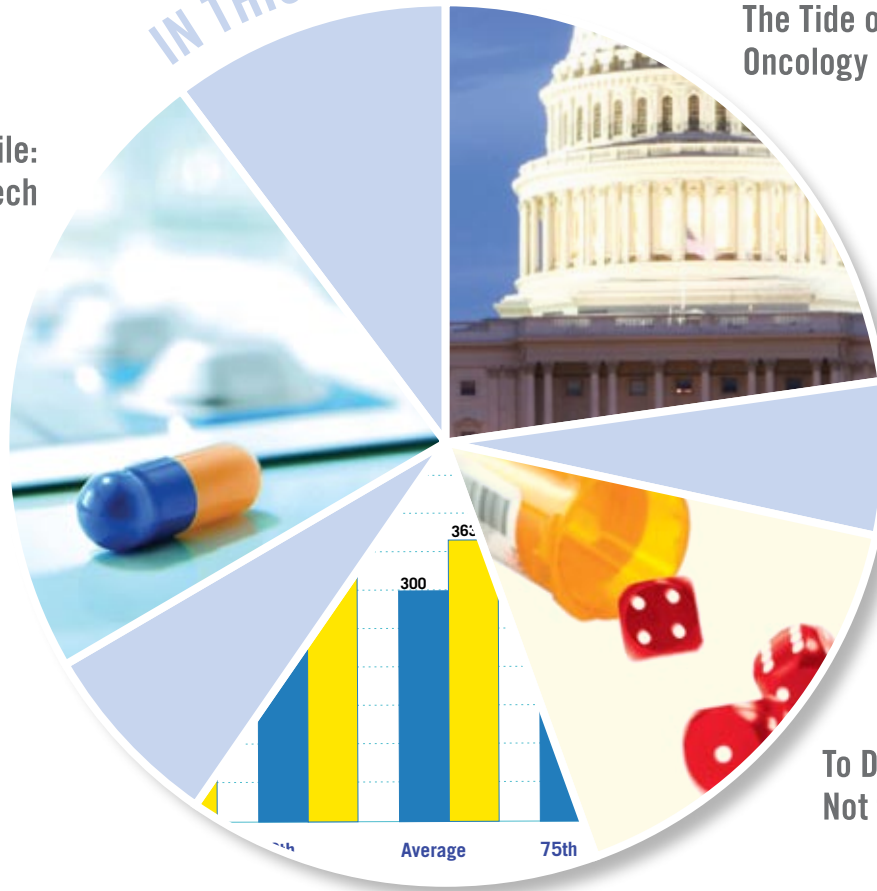
ONCOLOGY BUSINESS REVIEW

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GPC Biotech and the Satraplatin Story: Banking on Commercial Success with the Product That Almost Wasn't

By Diane S. Pena

The right study, the right environment, and the right company: It all adds up to big market potential for GPC Biotech and their oral chemotherapy satraplatin. Just where did this company come from and what are they all about? We delve into GPC Biotech as they build an infrastructure for the impending launch of their first product.



GPC Biotech (Nasdaq: GPCB) is betting the farm that its novel oral platinum-based drug satraplatin will establish the company as a commercial presence both in Europe and the US. By this time next year, GPC Biotech hopes that it will be sitting comfortably with revenues beginning to stream in from the first of several indications for its initial product, providing funding for its next decade of pipeline development.

In February 2007, GPC Biotech completed its new drug application for satraplatin for second-line treatment of hormone-refrac-

tory prostate cancer (HRPC). With the recent announcement that the FDA has granted priority review status to satraplatin, it looks as though the company has taken a major step toward its goal, with possible approval as early as mid-August.

If satraplatin is successfully brought to market, it will be the culmination of a long and winding road for this compound, and a vindication for those at GPC Biotech who believed in a compound that was abandoned by Big Pharma. **cont. on pg 24 >>**

GPC Biotech and the Satraplatin Story

Corporate History and Vision

GPC Biotech is a small biotech company with dreams of becoming a transatlantic player. Founded in 1997 as a spinoff of the Max Planck Institute for Molecular Genetics in Berlin, the company has made a series of strategic moves in an effort to develop the full spectrum of drug discovery, development, and commercialization capabilities. The acquisition of US biotech company, Mitotix, Inc. in 2000 gave GPC Biotech additional drug discovery expertise in the area of cell cycle inhibition, and helped provide a solid foothold in the US.

“To be successful in the long run, we recognized that companies need access to commercial and financial markets in the US,” CEO Bernd Seizinger, MD, PhD explained, noting that the large pool of often shorter-term investors in the US tends to balance the smaller pool of longer-term institutional and private investors in Europe. A US presence permits the company to draw on talent from both sides of the Atlantic. Today, approximately half the company is based in the US and half in Germany, and Seizinger divides his time between the two countries.

In 2005, the leadership at GPC Biotech saw another opportunity and acquired the assets of Axxima Pharmaceuticals, a kinase drug discovery firm based in Munich that was in bankruptcy proceedings. “The acquisition of Axxima gave us a very complementary set of skills and tools to our existing drug discovery organization,” said Seizinger.

The company has assembled a solid executive suite that includes Chief Medical Officer and Senior VP, Drug Development, Marcel Rozenzweig, MD, who was formerly Vice President, Infectious Diseases, Oncology and

Immunology Clinical Research at Bristol-Myers Squibb (BMS). In 2006, the company added Martine George, MD, formerly Senior Vice President, Head of Oncology at Johnson & Johnson Pharmaceutical Research and Development, as Senior Vice President, Clinical Development. An equally experienced commercial team is being led by Hemanshu Shah, Vice President, Commercial Operations, PhD, also formerly of BMS Oncology. Together, the team has a combined track record of over 25 NDA approvals.

Financial Picture

Like many small companies with big aspirations, GPC Biotech is facing the dilemma of how to fund development and commercialization with no current product revenue. The company presently holds approximately \$170 million in cash, cash equivalents, and marketable securities. For the 2006 fiscal year, it reported a net cash burn of about \$89 million. Cash burn can be expected to increase through 2007 as the company ramps up for commercialization of satraplatin. According to management, the company expects revenues to remain relatively stable through 2007.

To help underwrite development costs, GPC Biotech signed a 2005 agreement with Pharmion Corp., who will commercialize satraplatin in Europe. Through this arrangement, Pharmion has exclusive commercialization rights to satraplatin for Europe, the Middle East, Australia, and New Zealand, while GPC Biotech retains rights to the US, Canada, Japan, and all other markets. GPC Biotech has already received \$37 million from Pharmion to reimburse current and past development costs, and is entitled to royalties and milestone payments as satraplatin reaches regulatory

“To be successful in the long run, we recognized that companies need access to commercial and financial markets in the US...”

and commercial benchmarks in Europe and Pharmion's other territories.

Satraplatin: A Compound Overlooked by Big Pharma

The story of how GPC Biotech came to sublicense satraplatin illustrates the convergence

NeoTherapeutics (now Spectrum Pharmaceuticals), but the company found it lacked the resources to go full steam ahead with Phase 3 trials. In what Seizinger refers to as a bit of serendipity, Dr. Rozenzweig happened to meet an erstwhile BMS colleague, who had joined NeoTherapeutics after leaving BMS, at a party.



CEO Bernd Seizinger, MD, PhD

of clinical savvy, networking, and happenstance. Satraplatin had been licensed to BMS in the early 1990s and began early-stage clinical trials there. After a management change at BMS in the late 1990s, priorities shifted, and a decision was made to return satraplatin and several other compounds to their originators.

“There was nothing wrong with satraplatin—or with many of the other compounds. They just didn’t fit into BMS’s new genomics-focused vision,” noted Seizinger.

Johnson Matthey, satraplatin’s originator, then licensed the compound to

The topic of satraplatin came up, and within 2 months, the companies had worked out a deal giving GPC Biotech the right to develop satraplatin for commercial use.

“We recognized that satraplatin was a ‘diamond in the rough,’ said Seizinger. “This is not the first time that a compound overlooked by Big Pharma has found a good home in the hands of a nimbler, more focused biotech company.”

A platinum compound such as satraplatin may seem “old school” in the present era of genomics and targeted [cont. on pg 26](#) ➤

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therapies; however, platinum compounds have proved to be chemotherapeutic workhorses, with utility in lung, ovarian, bladder, colorectal, and other solid tumors. Satraplatin distinguishes itself from available platinum compounds—cisplatin [Platinol®; BMS], carboplatin [Paraplatin®; BMS], and oxaliplatin [Eloxatin®; Sanofi-Synthelabo]—by its oral delivery form and its activity in prostate cancer, a tumor type in which platinum compounds are not usually considered to be active.

By selecting second-line HRPC as an initial indication, the company hopes to address an unmet need and find the quickest route to approval and commercialization. Patients in the US with HRPC typically receive Taxotere® (docetaxel), the only approved treatment for metastatic HRPC that has shown a survival advantage. Inevitably, even those who respond to Taxotere experience disease progression. For these patients, there is a significant unmet need for effective therapies.

The company worked with investigators and the FDA to develop a rigorous protocol for the Phase 3 trial. The named trial, Satraplatin and Prednisone Against Refractory Cancer (SPARC), would hopefully satisfy regulators and be powered to demonstrate a clinically meaningful benefit. “In second-line HRPC, we saw the opportunity for a relatively quick registrational trial,” said Seizinger.

According to Dr. Oliver Sartor of the Lank Center for Genitourinary Oncology at the Dana-Farber Cancer Institute, co-principal investigator of the SPARC trial, GPC Biotech went to the FDA and got a Special Protocol Assessment (SPA) based on progression-free survival (PFS) as an endpoint. “This composite

endpoint has the advantage of being simple, measurable, and clinically meaningful.”

It is also consistent with historical endpoints used in past registrational trials for other agents. Progression events were reviewed by a blinded independent review committee, which included recognized experts in the field of prostate cancer. As Sartor noted, “It’s simply a good trial design.”

SPARC was conducted at 170 sites globally and included a total of 950 patients with HRPC that had progressed after previous chemotherapy participated. Investigators compared satraplatin plus prednisone with placebo plus prednisone.

For patients who received satraplatin plus prednisone, intent-to-treat analysis shows a statistically significant improvement in PFS ($P=.0000003$; see Figure 1). Patients also had a 33% reduction in the relative risk of disease progression (hazard ratio of 0.67; 95% CI: 0.57 to 0.77). The improvement in PFS increased over time, and was not affected by the type of prior chemotherapy patients had received.

In March 2007, additional results from SPARC presented at the 22nd Annual European Association of Oncology Congress in Berlin showed statistically significant improvements in pain response and prostate specific antigen (PSA) response among patients who received satraplatin plus prednisone. Patients who have not yet progressed continue to be treated under the SPARC protocol and are being followed for survival. Final overall survival results are expected in late 2007.

...the company may begin to see initial US sales revenue from sartraplatin by the end of 2007, pending FDA approval and launch.

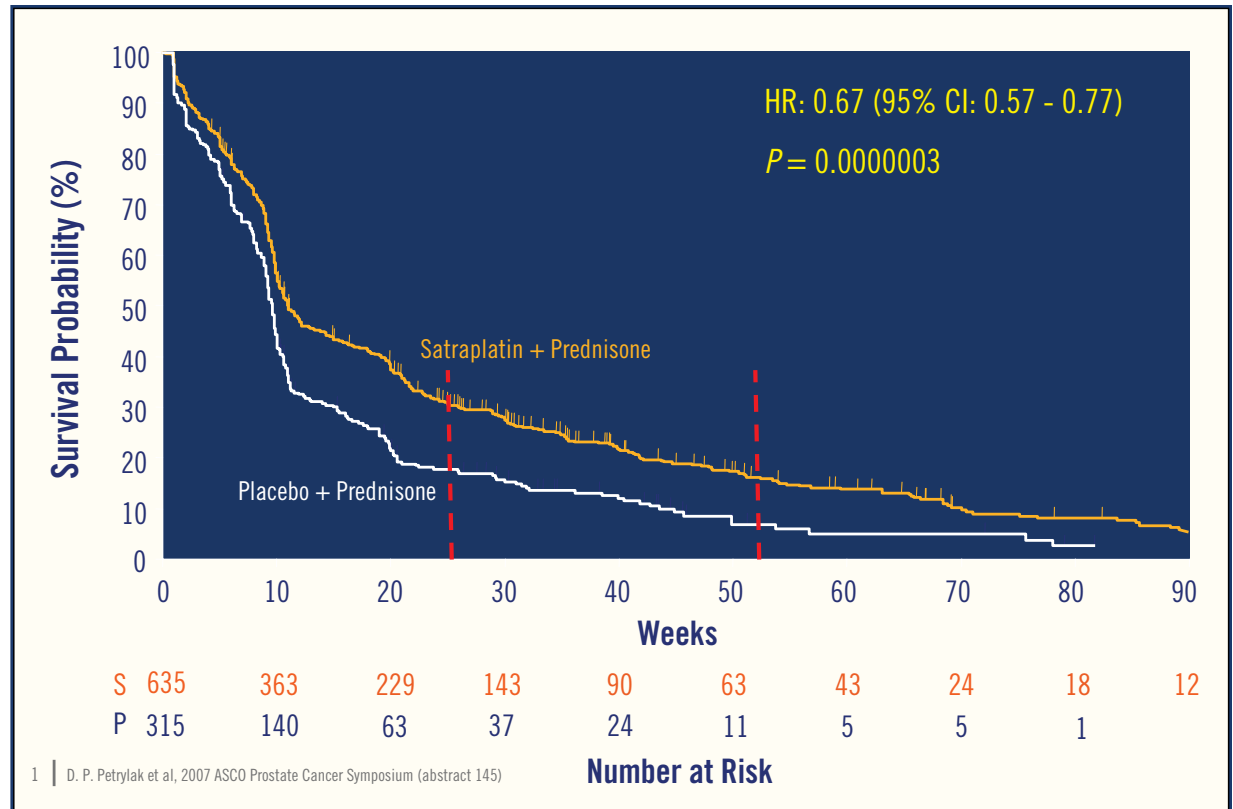


Figure 1. SPARC Trial: Progression-Free Survival Intent-to-Treat Analysis (per Independent Review Committee). Reprinted with permission.

The Investment Perspective

In the most optimistic scenario, the company may begin to see initial US sales revenue from satraplatin by the end of 2007, pending FDA approval and launch. According to Analyst Mark Monane, Needham & Company LLC, the company’s current cash level should last through 2008, or until satraplatin begins to generate revenues.

US sales of satraplatin could reach over \$500 million in peak annual sales. This estimate is based in part on worldwide sales of approximately \$2.2 billion for platinum-based drugs in 2005, a figure that is expected to grow. On

the basis of expected approval and anticipated commercialization of satraplatin, Needham & Company currently has a “Buy” rating for GPC Biotech.

This wasn’t always the case as the company has faced its share of skepticism from the investment community who doubted the wisdom of GPC Biotech moving forward with a compound that had been initially rejected by BMS.

But in 2003, when an analysis of data from a Phase 3 trial in first-line HRPc that been halted by BMS reported significant activity for satraplatin, the medical and **cont. on pg 28 >>>**

GPC Biotech and the Satraplatin Story



Figure 2: GPC Biotech 2-Year Stock Performance Chart. Source: <http://yahoo.finance.com/>

investment communities took notice of satraplatin—and GPC Biotech.

More recently, the upturn in stock prices in 2006 and early 2007 reflect the release of topline data from the SPARC study and ongoing incremental supportive data (see Figure 2).

Analyst Monane commented that with its Special Protocol Assessment, Fast Track Designation, priority review status from the FDA, and positive data from SPARC, the company is right on track for approval in second-line HRPC. “They’ve checked all the boxes and done all the right things for their initial NDA submission.”

With no other approved therapies for second-line HRCF, the initial market for satraplatin is wide open. Furthermore, satraplatin has several advantages over currently available platinum compounds. Its oral delivery method is expected to be embraced by patients and caregivers and other data suggest that the adverse events associated with satraplatin are relatively benign.

Dr. E. David Crawford, head of Urologic Oncology at University of Colorado Health Sciences Center (UCHSC), said that he sees no barriers to the adoption of satraplatin for second-line HRPC, noting that “it’s the first time anything has been shown to have activity in second-line HRPC.” He sees oral administration as a big advantage for patients and physicians, particularly in outpatient settings, where many urology physician offices are not equipped to handle infusions. He also commented that he looks forward to seeing the development of studies in first-line HRPC and even earlier in the disease process.

Facing Obstacles and Risks

As is always the case in biotech, risks abound. Final results from SPARC may fail to bear out the promise of preliminary findings, or the FDA may not like what it sees. Commercialization poses another hurdle—like many small biotech companies, GPC Biotech has never commercialized a product before. Nonetheless, as Monane notes, the company is rich with talent. “Its management team consists of proven winners with an extensive track record at BMS and other Big



Another challenge facing the company is the fact that US patent protection for satraplatin is due to expire within a few years...

Pharma and biotech companies. These folks are very smart, designed a good trial, and I think they'll continue to make smart decisions going forward."

Another challenge facing the company is the fact that US patent protection for satraplatin is due to expire within a few years; the composition of matter patent expires in December 2008 and the medical use patent expires in September 2010. The company intends to file for a Hatch-Waxman patent term restoration, which, if granted, would provide coverage as late as September 2015, depending on which patent the company chooses to apply it to. (In Europe, satraplatin will be protected for 10 years after EMEA approval.) This factor obviously increases the impetus for getting satraplatin on the market as quickly as possible.

Finally, there is a bit of unfinished business between GPC Biotech and Spectrum Pharmaceuticals (formerly NeoTherapeutics). Spectrum alleges that it is entitled to approximately \$12 million from the total payments received by GPC Biotech from Pharmion for past and ongoing satraplatin development costs; GPC Biotech, in turn, has said that Spectrum's claims are baseless and were made in bad faith. The matter is headed to arbitration; however, Monane considers the risk to investors to be slight, because the amount involved is relatively small and likely to be resolved soon. (Under the original sub-licensing agreement, Spectrum is entitled to low double-digit royalties on worldwide sales; this is not under dispute.)

The Future of Satraplatin: Niche Product or Blockbuster?

While second-line HRPC provides perhaps the shortest and most direct route to approval and commercialization for satraplatin, it represents only a relatively small part of the potential market for the drug. For GPC Biotech to succeed, the company must show that satraplatin performs well in other indications and can compete against other approved therapies.

To this end, the company plans an ambitious program of clinical trials studying satraplatin in combination with other therapies and in various cancer settings. In general, platinum compounds do not demonstrate the cross-resistance that plagues many other cancer therapies, such as taxanes, meaning that satraplatin may be useful regardless of the previous treatment a patient has received, and may be active when deployed in combination with these agents.

There is also excitement about the prospect for using satraplatin in combination with radiotherapy, because of platinum compounds' known ability to potentiate radiation therapy. A Phase 1/2 trial of radiotherapy plus satraplatin has already begun in NSCLC.

An oral compound like satraplatin may have particular advantages in combination with radiation therapy. Delivering radiotherapy with an intravenous platinum compound can be a logistical nightmare. Not only is the radiotherapy schedule demanding for the patient, but it provides only a relatively small overlap when the patient is receiving both the platinum and the radiotherapy. "With satraplatin, the patient can take the cap- **cont. on pg 30 >>**

GPC Biotech and the Satraplatin Story

sules and then go to radiation therapy, and, hopefully, get the full benefits of the synergy,” explained Seizinger.

It is interesting to note that BMS may have cast aside satraplatin, at least in part, because of concerns about its commercial potential as an oral anticancer agent. At that time, oncology practices depended on the profitability of IV chemotherapy to sustain their business, and it was believed that oral chemotherapy agents would not be welcomed. As the reimbursement environment has shifted to less profit on the drug itself and more reimbursement for administrative services, IV agents have become less profitable and the opportunity for oral chemotherapy has grown. It also helps that many successful oral anticancer therapies have been launched with widespread acceptance and that reimbursement for these agents has been formalized. Seizinger noted that the timing for satraplatin may finally be right.

The Competitive Landscape

On the competitive horizon, the potential approval of Dendreon’s Provenge® vaccine for first-line HRPC is unlikely to affect adoption of satraplatin. Provenge is likely to be approved for first-line use in asymptomatic patients with metastatic HRPC. As Crawford of UCHSC explained, if Provenge and satraplatin are both approved, a likely scenario in patients with HRPC might be Provenge, followed by Taxotere and then satraplatin, or perhaps earlier use of satraplatin if supported by the data. Given that the toxicity profiles of Provenge and satraplatin do not overlap, the possibility for combining the two agents, or using them in sequence, exists.

Table 1. Products in Development for Prostate Cancer

Taxotere (docetaxel)-based combinations
• Taxotere plus vinorelbine
• Taxotere plus bevacizumab
• Taxotere plus calcitriol
• Taxotere plus satraplatin
• Taxotere plus oblimersen
Immunotherapies
• Provenge® (Dendreon)
• GVAX® (Cell Genesys)
• PROSTVAC® (Therion)
• PSMA (prostate specific membrane antigen)-directed therapies (various)
Cytotoxic therapies
• Ixabepilone (BMS)
• Ispinesib (Cytokinetics/GSK)
• Halichondrin B analog (Eisai)
Targeted therapies
• Bevacizumab (Avastin®, Genentech)
• Sorafenib (Nexavar®, Bayer)
• Atrasentan (Xinlay™, Abbott)
• Sunitinib (Sutent®, Pfizer)
• Imatinib (Gleevec®, Novartis)
• Bortezomib (Velcade®, Millennium)

“A company with a \$500 million drug is a good story...But a company with a \$500 million drug, plus another in the pipeline, is a better story.”

While there is no direct competitor for satraplatin immediately on the horizon, HRPC continues to be a major focus of oncology research, and treatment paradigms for HRPC may shift as new therapies and regimens emerge. In particular, investigators are evaluating docetaxel-based combinations (including docetaxel plus satraplatin) for first-line treatment of HRPC (see Table 1).

Pipeline Issues

To ensure its long-term success, GPC Biotech must demonstrate that it is able to build a broader, deeper pipeline. As Monane noted, “A company with a \$500 million drug is a good story...But a company with a \$500 million drug, plus another in the pipeline, is a better story.” He cites Celgene as an example of a biotech company that has built its company on two strong products: Revlimid® (lenalidomide) and Thalomid® (thalidomide).

GPC Biotech hopes to move into Phase 2 development in 2007 with its first anticancer compound developed in-house, 1D09C3, a monoclonal antibody compound which has shown activity in vitro against a variety of T and B cell cancers. It is presently being studied in patients with relapsed or refractory B-cell lymphomas, such as Hodgkin’s disease and non-Hodgkin’s lymphomas, including chronic lymphocytic leukemia (CLL).

Investors may wonder whether a pipeline consisting of an oral platinum compound, a monoclonal antibody-based drug, and a handful of kinase inhibitors in preclinical development adds up to a strategic vision for the company. Seizinger thinks so. He believes that the future of cancer treatment lies in combination therapies, using compounds with

different mechanisms of action, and capitalizing on synergies.

With approximately 120 scientists involved in its internal drug discovery effort, the company is looking at small molecules and monoclonal antibodies, and its earlier programs are focused on kinase inhibitors.

“These are the areas where we have strong expertise,” said Seizinger who also noted that the company is open to the possibility of licensing additional compounds or partnering with other companies with compounds in late-stage development as it waits for its in-house drug development program to mature.

What’s ahead for 2007-2008

In the coming year, the company expects to release final survival data for SPARC and anticipates a decision from the FDA as early as mid-August. While the company plans to be ready to promote without a partner in the US, they have not ruled out the possibility of partnering with another company.

Recently, the company announced it will consolidate its drug discovery efforts to Munich, Germany, and close its Waltham, Mass. office. Meanwhile, the Princeton, NJ site is expected to grow as preparations continue for the commercialization of satraplatin in the US. This involves developing sales and marketing staff, establishing distribution channels with specialty pharmacies, setting up programs to monitor compliance, and working out potential reimbursement issues. **DSP**



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