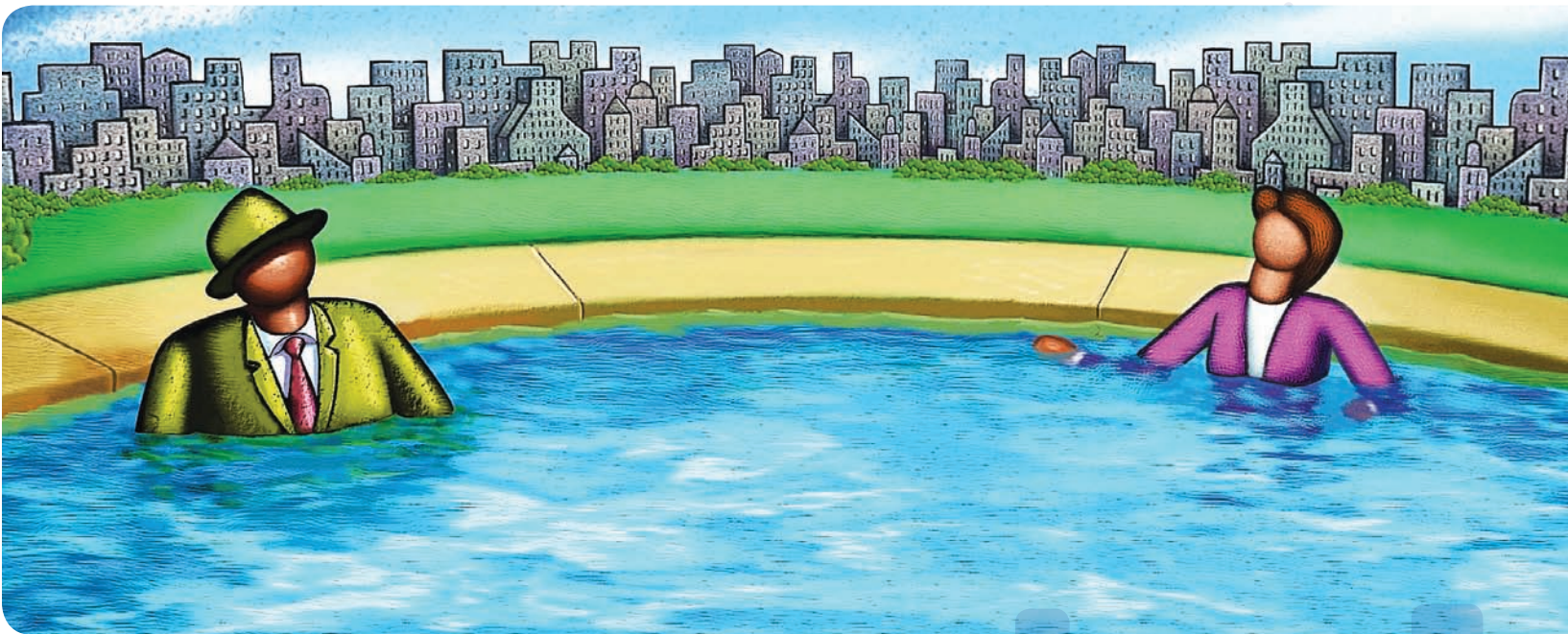




# Competitive Landscape: *Designing the Next*

By Linda Stanley





Speakers from the 2006 Bio InvestorForum Meeting discuss strategies on entering the marketplace and how to navigate through the stiff competition of oncology drug development.

# Cancer Drugs

More new drugs with novel activity are vying for oncology indications than ever before. While the most desirable strategy is to establish a new product as the standard of care, the cost of trials against so many competitors is often prohibitive. Add to this the scrutiny of payors and patients who are changing the standards of efficacy, and new drug development becomes a formidable challenge.

The 2006 BIO InvestorForum, held in October in San Francisco, explored how such stiff competition is changing the market. Jason Kantor, PhD, analyst with RBC Capital Markets, moderated a panel of executives from four leading biotech companies, who discussed their strategies for developing successful products, establishing them as standard of care, and defending their positions from new competitors (see box for participants).

For three of these companies, deciding where to enter the marketplace is a key component of

marketing strategy. They hope that targeting multiple patient segments will offer the best return.

Sunesis Pharmaceuticals has pursued this philosophy with two of its small-molecule oncology products: SNS-595 and SNS-032. Both products are inhibitors of the cell division process, and are known as cell-cycle inhibitors. SNS-595 is in Phase II trials for advanced small cell lung cancer (SCLC) and nonsmall cell lung cancer (NSCLC), as well as in Phase I trials for hematologic malignancies. SNS-032 is in Phase I trials for a broad range of advanced solid tumors including breast, NSCLC, and melanoma. These products act on more rapidly dividing cancer cells rather than quiescent normal cells.

Donald Swisher, President and CEO of Sunesis, explained one of their strategies is to look for entry into areas where platinum or taxane resistance creates an unmet need. "We target areas where these agents are standards and follow in second-line," said Swisher. "One of the benefits with refractory cancer is that you can conduct single-arm trials for approval."

Sunesis phase I data have opened up the possibility of pursuing an indication for treating ovarian cancer, and evolving preclinical data for acute myelogenous leukemia show profound synergy with ara-C. Swisher emphasized that quickly moving a new drug to proof of concept is critical. He stated that while cancer therapies have fallen out of favor with investors, most of the new products are geared to diseases that are far from cured.

Seattle Genetics is also pursuing multiple entry points for one of its [cont. on pg 18 >>](#)



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monoclonal antibodies, SGN-40, which is in Phase I/II trials. SGN-40 is a humanized antibody that targets the CD40 antigen. Receptors for CD40 were originally discovered on bladder cancer, but they are also expressed on hematologic malignancies, such as multiple myeloma (MM), non-Hodgkin's lymphoma (NHL), and chronic lymphocytic leukemia (CLL). Renal and ovarian cancers also express this antigen.

Clay Siegall, President and CEO of Seattle Genetics, said that with SGN-40, they are targeting tumors in several large markets, where there are few options for aggressive disease. These include NHL, MM with 16,000 patients annually, and CLL with 10,000 patients annually. Although new products have extended survival somewhat for MM and CLL, there is still no cure. According to Siegall, there are multiple pathways open for SGN-40 from front-line to third-line.

As a single agent, SGN-40 produced five objective responses in a Phase I trial for all stages of relapsed/refractory NHL. Four of these responses were in aggressive NHL. A Phase II study is planned to start in the next month. Siegall noted that NHL is a heavily CHOP-dominated (cyclophosphamide, doxorubicin, vincristine, and prednisone) market. "SGN-40 works well with combination CHOP therapy. Our future goal is to be established as front-line therapy, improving CHOP as well as CHOP/Rituxan® therapy."

Another pathway possibility involves combination with Rituxan plus Isor (Rice-IS) for second-line treatment and SGN-40 plus Rituxan as third-line treatment.

Strategy at AdventRx focuses on linking a product to—and improving—foundational

therapy. CoFactor®, the active moiety of leucovorin, is a biomodulator that enhances fluorouracil (5-FU). It is currently in Phase II/IIb trials as first-line therapy for the treatment of metastatic colorectal cancer. Leucovorin in combination with 5-FU has been the standard of care for a number of years. Trials are showing significantly reduced toxicity with CoFactor and 5-FU.

According to James Merritt, MD, President and Chief Medical Officer at AdventRx, there have been no grade 3 or 4 toxicities in trials, and the hematologic toxicity is well below 10 percent. Anticipated rates for a leucovorin/5-FU regimen are around 15 percent. Merritt said, "5-FU is truly the backbone of therapy. Even as newer agents have been developed, 5-FU has not been eliminated, and it's still used in first-line through third-line treatment."

Improvement in this facet of therapy carries great potential, as is evident in the size of the leucovorin market—about \$400 million worldwide and growing.

Front-line treatment with CoFactor/5-FU proved beneficial through second-line therapy as well. After patients completed the industry-sponsored Phase II trial, their physicians selected various second-line therapy including FOLFIRI (5-FU, leucovorin, irinotecan), FOLFOX (5-FU, leucovorin, oxaliplatin), and Avastin®. The 33 patients who went on to some form of second-line treatment had an overall survival of 23 months, which is slightly better than the best comparator in the literature. Merritt found this data exciting, because it implies that you can use the less toxic CoFactor regimen first and defer the greater toxicity until later.

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In contrast to these companies, Genentech—the biotechnology giant—faces the challenge of maintaining products as standard of care. John Orwin, Vice President, Marketing and Sales, BioOncology, observed that their key commercial strategies are “to establish, expand, and defend.”

“As a market leader, our goal would be to leverage our position through marketing and sales by capitalizing on our unique consultative selling approach,” stated Orwin. He explained that their strong customer relationships combined with patient access programs help achieve their goal. With four oncology products approved by the Food and Drug Administration (Avastin, Herceptin®, Rituxan, Tarceva®), any number of ongoing trials to expand their indications, and several new entities in the pipeline, Genentech looks impenetrable.

Orwin indicated that sales of Avastin for the first nine months of 2006 were \$1.25 billion and climbing. But he pointed out that many of the new products—and new technologies—represented by the panelists are direct competitors hoping to erode Genentech’s market share.

Defending Avastin, for example, has involved establishing the importance of the mechanism of action. It is an anti-VEGF antibody used in combination with 5-FU-based therapy (first- or second-line) for metastatic colorectal cancer and in combination with carboplatin and paclitaxel for the first-line treatment of advanced, recurrent or metastatic nonsquamous NSCLC. This later indication was only recently approved by the FDA in October 2006, pointing to another important defensive strategy. Orwin says the company develops a life-cycle strategy for each product by planning expan-

sion of indications and is exploring other solid and hematologic malignancies with Avastin across all lines—first-line, adjuvant, relapse/refractory. The company plans to combine Avastin with other targeted therapies in and outside the Genentech portfolio.

Elimination is not necessarily the goal with competitors. Swisher hopes that competitors set the bar higher and look at products either in combination or in head-to-head trials. However, with so many new competitors, Kantor asked if there could be a breaking point in the system, for example with SGN-40 and Rituxan. For SGN-40, innovation to prevent this splintering of the market involves addressing price and setting a reasonable value for the initial indication.

Siegall believes that it is important to be flexible and innovative in setting price, because it is impossible to know how many additional indications—at what dosages—will be added. “We need to be careful about making a pricing decision at the time of launch that is prohibitive.”

Another factor that complicates new drug development is the changing standard for proving efficacy. Some criteria involve progression-free survival, and others use overall survival. In refractory patients, efficacy is measured by responsiveness. Orwin noted that payors will pay for effective drugs, but with so many competitors, it is increasingly expensive to prove a clear advantage: “The more drugs you have to put in a trial, the more you reduce your ability to clearly show a difference.”

He feels that quality of life is also entering the picture in terms of efficacy. “For decades we have used the [cont. on pg 20 >>](#)

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mantra that the more toxic the better, but this is finally shifting.”

Each new indication for a product requires an increasing number of trials. This escalates the cost of development and fragments the market into narrower pathways. It also leads away from the traditional definitions of cancer to smaller subsets of patients with similar histology or patient factors. Such market

fragmentation has raised the cost and complexity of achieving clinical proof of concept, and it is somewhat counter to the goal of broad adoption. The breaking point Kantor alluded to is the potential for market growth. Can the size of the oncology market increase indefinitely, or will the “gold rush” oversaturate the market? **IS**

## PARTICIPATING COMPANIES

Company	Financial Profile	Product/s Discussed	Development Stage
<b>AdventRx</b>	Symbol: ANX Market Cap: \$181.65M Closing Price Nov 15: \$2.64 52 Week Range: \$2.32 – \$5.38	<b>CoFactor® (ANX-510)</b> • Biomodulator that enhances 5-FU cancer therapy	Phase III (US) • 1st line tx metastatic colorectal cancer Phase IIb (Europe, India) • 1st line tx metastatic colorectal cancer Phase II (US) • 1st line tx metastatic colorectal cancer with 5-FU
<b>Seattle Genetics</b>	Symbol: SGEN Market Cap: \$269.93M Closing Price Nov 15: \$5.48 52 Week Range: \$3.80 – \$5.97	<b>SGN-40</b> • humanized antibody targeted to the CD40 antigen  <b>SGN-30</b> • humanized antibody targeted to the CD30 antigen	Phase I • multiple myeloma, non-Hodgkin's lymphoma Phase I/II • chronic lymphocytic leukemia  Phase II • systemic anaplastic large cell lymphoma (ALCL), cutaneous ALCL
<b>Sunesis</b>	Symbol: SNSS Market Cap: \$139.18M Closing Price Nov 15: \$4.65 52 Week Range: \$4.14 – \$7.40	<b>SNS-595</b> • cell-cycle inhibitor that inhibits cell division  <b>SNS-032</b> • cell-cycle inhibitor that inhibits cell division	Phase II • Advanced small cell lung cancer • 2nd line tx advanced non-small cell lung cancer Phase I • Acute lymphocytic leukemia, acute nonlymphocytic leukemia, chronic myeloid leukemia, myelodysplastic syndromes  Phase I • Advanced solid tumors: breast, non-small cell lung cancer, melanoma
<b>Genentech</b>	Symbol: DNA Market Cap: \$85,870M Closing Price Nov 15: \$80.44 52 Week Range: \$75.58 – \$100.20	<b>Avastin®</b> • Anti-VEGF antibody	FDA approved • In combination with IV 5-FU-based chemo for 1st or 2nd line tx of metastatic colorectal cancer • In combination with carboplatin and paclitaxel for 1st line tx of unresectable, locally advanced, recurrent or metastatic non-squamous cell lung cancer