

## Daniel Swisher, CEO and President, Sunesis Pharmaceuticals Inc., South San Francisco, CA



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In the fight against cancer, Sunesis Pharmaceuticals (Nasdaq: SNSS) is an emerging biotech that is building a pipeline of drugs that selectively blocks critical mechanisms required for tumor growth and survival. Founded in 1998, consisting mostly of chemists and biologists, Sunesis focused its research on creating and refining its Tethering platform, which enables

the company to discover lead molecules by identifying and combining fragments that bind to a site of interest on a target. SNS-595 is their lead compound and it is being explored in ovarian cancers and in acute myeloid leukemia. Other compounds in their pipeline include SNA-032, a selective inhibitor of cyclin-dependent kinases 2, 7, and 9 for B-cell malignancies; and SNS-314, a selective inhibitor of aurora kinases A, B, and C for advanced solid tumors. The following is an excerpt from an interview OBR conducted with Daniel Swisher, CEO and President.

**OBR:** *Can you provide some insight as to who Sunesis is as a company?*

**DS:** When I joined in 2002, Sunesis was a 4-year old venture-backed company. The founder hailed from Genentech, and his insight was that the biggest Achilles' heel in the pharma world is the lack of productivity in small molecule drug discovery. At the time when I joined, we were covering six therapeutic areas so to me, our first challenge as a company was to transition from a technology platform to a therapeutic platform. We put the stake in the ground so to speak with oncology.

**OBR:** *Why did you select oncology?*

**DS:** We felt that with the insights on emerging biological targets there ought to be more elegant ways to discover small-molecule drugs. So we developed a fragment-based platform where we could discover drugs in pieces that are really site-directed to a disease target of interest. Our drug discovery efforts are directed at kinases—as they play an essential role in many of the signaling pathways that drive tumor survival and growth. Tethering, our discovery technology, is ideally suited for identifying highly-selective and novel inhibitors of protein kinases. Because of our technology, we can design drugs that go outside of the normal ATP binding pocket which is highly promiscuous among all kinases. As a result, we can limit off-target toxicity and generate novel IP in a competitive field.

**OBR:** *What is SNS-595, your lead compound?*

**DS:** We found SNS-595, in Japan. The compound targets DNA during cell replication and has a mechanism of action that includes inhibition of Topoisomerase II which, during replication, helps chromosomal DNA unwind so that it can be copied. SNS-595 traps Topoisomerase II that is bound to the DNA, which causes the DNA to break and as a result undergo programmed cell death. We also know that SNS-595 acts only on the dividing cells while not having any cytotoxic effect on normal non-dividing cells.

What's really impressive about SNS-595 is its breadth of pre-clinical and emerging clinical activity. It appears to work in disease-resistance settings and has great pharmaceutical properties. Cytotoxics, as we know, are not going to go away, but they're going to get combined with newer biologics and targeted therapies.

**OBR:** *What have your clinical trials revealed?*

**DS:** In Phase 1 clinic settings of about 100 patients, SNS-595 has demonstrated activity and a very clean side-effect profile. The only toxicity we saw of note for solid tumors was neutropenia; we saw no cardiotoxicity or neurotoxicity. So we are taking that experience and going in two directions. One is in a solid-tumor Phase 2 study in ovarian cancer and the other is in a Phase 2 liquid tumor setting in acute myeloid leukemia. We shared some positive response data in AML at last December's ASH meeting and we're currently on the verge of getting more efficacy data and we could see data at ASCO '08 for the ovarian studies.



**OBR:** *What is your clinical strategy?*

**DS:** In solid tumors, we've also seen initial activity and durability of response in patients with platinum-resistance. Studying SNS-595 in ovarian cancer, we can go one of two ways: (1) platinum-resistance disease pre-Doxil and go for something better than Doxil or (2) if the trend holds up in patients failing Doxil go up against best supportive care.

In AML, our current clinical strategy is to take the Phase 1 dose and move into elderly AML patients who are not good candidates for the current combination therapy available. If that signal is positive, we stay competitive relative to clofarabine and cloretazine, and we can push into a registration study next year. That's for first-line elderly patients with AML patients who are unfit for traditional chemo—about one-third of the newly diagnosed AML patient population.

Two-thirds of the same patients population generally get the seven plus three (Ara-C/daunorubicin) regimen and if they fail within a year they usually get challenged with high-dose Ara-C. In this setting, we're looking at combining with Ara-C. Then we do a plus or minus study in that patient population and look for additional clinical benefit without significant additional toxicity.

**OBR:** *What is your business strategy for SNS-595?*

**DS:** We hope to have data mid-year which can lead to our pursuing one or more registration strategies and explore entering into broader partnerships. We want to partner from a position of strength with Phase 2 data in hand. We would like to hold on to North American rights so that we have significant upside potential when SNS-595 becomes a drug and directly participate in the top-line sales revenue. But we also know that we need the help of a large partner to develop the compound broadly and go through the regulatory process on a global basis.

**OBR:** *How competitive is the AML market?*

**DS:** Five years ago, MDS wasn't considered a viable commercial market and now people think it's going to soon be a billion dollar market. AML has that same opportunity. If Ara-C was priced as a branded product it would be a \$500M to \$1B drug.

What's interesting in the AML market is that most of the competition is pursuing drugs that are iterations of the cur-

rent chemo standards. It's a competitive area, but honestly, all of the cancer areas are competitive and the angle we have with SNS-595 is a unique mechanism with a broad therapeutic window.

**OBR:** *What other products do you have in your pipeline?*

**DS:** SNS-032 is a compound we have that is being studied in patients with CLL and multiple myeloma. In Phase 1 studies, SNS-032 is showing potent anti-tumor activity. It inhibits the phosphorylation of CDK 7 and 9 substrates, reduces RNA synthesis, and induces apoptosis in CLL cells. Also in the Phase 1 trial stage, in patients with advanced solid tumors, is SNS-314. That compound has shown additive effects in combination with standard anti-cancer treatments. It is a potent inhibitor of all 3 aurora kinases, A, B, and C.

**OBR:** *Sunesis' stock dipped last year – please explain.*

**DS:** Micro caps were down about one-third last year, across the board. We were down a little more than that for a couple of reasons. One was we did an offering in late spring and some of our investors were not long-term investors so they flipped the stock. We don't get traded a lot so it put a lot of pressure on the stock price.

The other factor is we made some tough portfolio decisions on our programs and stopped a couple of trials with SNS-595 in lung cancer so we could focus more on ovarian cancer. While that was the right long-term move, the market interpreted this as a signal that we didn't have confidence. And, until we can show the data and prove that ovarian cancer was the right move to take, there remains significant market skepticism. But by the time ASCO '08 rolls around we should have the data to show that it was the right thing to do.

**OBR:** *Any final take-aways you would like people to know about?*

**DS:** As a company, our challenge is to drive the clinical data that gets recognized by investors, but also bridges to strategic collaborations so that we can access less dilutive partner capital, but do it in a way that we haven't mortgaged our future. About 70% of our development investment is going into SNS-595 so this is a pivotal year for us to demonstrate the viability of the registration pathways for SNS-595. We're running five clinical trials across our three development programs in the clinic this year and we'll have results from all five, which provides significant upside. I think people's perception of Sunesis will change by the end of 2008.

