

The Birth Of A Baby Blue



It May Be The Most Important Biotech Ever

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Biotech's Blaze Begins to Cool at the Edges

To those of us who stand on the outside, the world of biochemistry blazes with amazing potential.

Biotech became even more exciting in 2006 when scientists announced they had mapped the last DNA sequence for the last of the 24 human chromosomes. The whole human genome map was done—the scientific achievement of the century. And it was biotech's own baby.

Miracles come from biotech. It's gospel. Big profits come from it, too.

Amgen went from 9 cents a share to \$80 a share...

Gilead Science from 56 cents to \$53...
Celgene from 62 cents to \$75...

I could keep going. Dozens of companies have topped 1,000% profits for investors. We'd all like to find the next one. It's out there, but one thing you should know. The Wild West days of biotechs are over. Investors were indiscreet in their enthusiasm.

Now they're sobered. Only a few extremely able companies are going to give investors 1,000% or better returns.

The problem is pipeline. And financing. But mostly pipeline.

But There's Still Heat at the Center

We are now entering the second phase of biotech investing after the human genome was mapped. In the 1990s and early 2000's, an enormous amount of new drugs and therapies came about quickly in this young field.

From now on, new discoveries will be rarer. Enthusiasm is tempered and investors are less free with their cash.

But amid the gloom about thin pipelines, I heard something else. Excitement under the caution. Biotech still has its darlings.

Inside the world of biotech, a lot of people already know who the next big winners are likely to be. These are the companies that everyone wants to work for, the companies industry insiders talk about.

I quizzed biotech scientists, strangers, friends of friends and asked who they admired, who's got "pipeline."

I expected everyone to say Genentech (this was before Roche bought it). Maybe Amgen or Biogen Idec. But the

one name that kept coming up alongside the billion-dollar leaders—was a baby blue-chip biotech company, Seattle Genetics (SGEN).

The Birth of the Baby-Blue Bio

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It started operations in 1998 and became a public company listed on Nasdaq in 2001.

Now the company has almost 300 employees on its Bothell, Washington, campus near Seattle.

From the beginning, it has concentrated on engineered monoclonal antibodies (mAb's) in the treatment of cancer and autoimmune diseases.

Already starting to quail?

A Therapy that Mimics A Healthy Body Helping Itself

OK, this much is fairly simple. When you have a disease that involves a bacterial or toxic attack (an antigen), your body responds by making antibodies. Antibodies fight antigens.

Antibodies are made of sequences of protein molecules. To explain how they work in very simple terms, they are often likened to a puzzle that fits to another puzzle piece. (Actually, they are Y-shaped, but puzzle pieces will do for us lay folk.)

Every antibody has a specific antigen target. They are created by the body to respond only to specific threats.

Antibodies may kill the invading foreign antigen outright. Sometimes they work by neutralizing an antigen or preventing it from multiplying. Or they may simply set conditions for other physical processes (such as a fever) to handle the problem.

When you go to the doctor and get a dose of antibody-based treatment, however, you are not usually getting antibodies created by another human kind enough to lend some of his to everyone else. We don't inject people

with diseases so they can be antibody farms.

Most antibodies are cultured in the lab or produced from the bloodstream of a small animal, like a lab rat, that was injected with an antigen such as a cancer cell.

These antibodies form powerful therapies, but they have limits scientists have been working to overcome for decades. This is where Seattle Genetics comes in. Its humanized antibody therapies look to be on track to solving a problem that has long vexed scientists in searching for antibodies strong enough to fight cancer.

This is Better than Science Fiction— What Do You Get when You Cross a Mouse with a Human?

One problem with fighting disease with antibodies is that even if a protein sequence from a human cancer cell is injected in a mouse, the antibody that is created will be a mouse antibody.

That means they will be greeted as foreign material by human bodies, even if they are doing good work.

That's why murine (mouse-derived) antibodies often get just one shot at working before the human taking them begins to develop antibodies to the foreign mouse content in the medicine.

That makes murine antibodies useless for repeated dosages.

To overcome this problem, scientists have learned to alter these animal-based antibodies to make them more acceptable. They may be "chimeric" or "humanized." Chimeric versions fuse human sequences of antibody proteins to the portions of mouse antibodies that relate to the target problem. The mix is usually about 30% mouse and 70% human protein sequences.

This was still short of the goal. So scientists went further to "partially humanized" (up to 90% human sequences) or fully-humanized" antibody production.

Unfortunately, as scientists humanized these antibodies, they often became less effective.

Seattle Genetic's research is done on this frontier with partially humanized or humanized antibodies it has

patented—including antibodies that Seattle Genetics has taken a step further as I'll explain.

How to Make a Partially Human Antibody

When you hear the term monoclonal antibodies, mAb, this is the kind of thing they are talking about—the .

The purpose of monoclonal antibodies is dual. They are chimeric or humanized to reduce the problem of rejection, as just described.

And they are produced repeatedly with every single cell being identical from batch to batch. This is accomplished by joining cells from a mouse that has been immunized with the cells from a target antigen. In Seattle Genetics' case, cancer antigens. This yields batches of monoclonal antibodies, highly controlled, consistent and predictable.

Seattle Genetics drug candidates And perhaps the vehicle that will someday carry a payload right to cancer cells and no others.

That brings us to the antibody drug conjugate (ADC)—biochemistry's "magic bullet.

The mAbs are genetically engineered antibodies, but ADCs go another step. A linker toxin binds a payload of toxin to the antibody. The antibody seeks out the target antigen, then the toxin is released to kill it.

And that's what's going on at Seattle Genetics now.

This is why Seattle Genetics is the most exciting company in biotech right now.

The Pipeline

A thin pipeline is no problem here. Seattle Genetics not only has multiple drugs in trials at the moment, it has the interest and backing of major drug companies that are interested in its work.

This is an important safety factor to you as an investor. Seattle Genetics is a rarity. It is a small, new biotech with no approved drugs so far that is actually making money because big drug companies are licensing its ideas and investing in it.

To give you an idea of how revolutionary these therapies are, consider this. So far the FDA has approved only five mAb drugs for cancer treatment. Period.

A Quick Take on Monoclonal Antibodies

This comes from textbook publishers Brooks Cole, a better explanation than I can give:

Typically, antibodies are generated using monoclonal antibody technology, which can produce large quantities of a mouse antibody that has singular specificity for a protein to which it was designed to bind.

Basically, the target protein (termed an antigen) is injected into a mouse, and when the mouse has developed a sufficient immune response to the antigen (including many protein-specific, antibody-producing B cells), its spleen cells (containing B cells) are harvested and fused to myeloma [cancer] cells. Myeloma cells are an immortal cell line that will allow the fused cells to grow indefinitely and at a fast rate.

These myeloma-B cell hybrid cells are called hybridoma cells, and can be selected for and tested to verify that they produce the desired antibody. The hybridoma clones that produce the antibody demonstrating the required specific binding activity can then be grown in large quantities, and the monoclonal antibodies can be harvested for use in an immunotoxin.

Seattle Genetics is working on two more promising candidates (Dacetuzumab, or SGEN-40, and an unnamed SGEN-70). Both are doing well so far in Phase I trials.

Seattle's First Drug Could Reach Market Soon

The world's first ADC drug was not approved until 2000. Seattle Genetics already has three additional ADC drugs in formal trials and a fourth one in pre-clinical testing. This is where the breakout is likely to come that will make Seattle Genetics a well-known name.

Its ADC Brentuximab Vedotin (SGN-35) is now in four separate Phase II and Phase III trials and two more Phase I trials. This is likely to be the first of the Seattle Genetics therapies to reach the market. In fact, it's very possible that Seattle Genetics will file a New Drug Application for Brentuximab vedotin sometime this year, probably in the first half of 2011.

This drug is aimed at treating the forms of cancer that fall under the Hodgkin lymphoma (NL) category. It may also be of value in some other types of cancers that have similar genetic patterns.

IN addition to the drugs already mentioned, Seattle Genetics also has two more ADCs in early trials for renal (kidney), prostate and pancreatic cancer.

This is a huge pipeline for a little company.

Seattle Genetics Pipeline

SGN-40. humanized mAb. Trials are addressing non-Hodgkin's lymphomas and multiple myelomas.

SGN-33 (limtuzumab). This is a humanized mAb (note the -mab ending on lintizamab, that's an indication that the drug is a monoclonal antibody). This drug is targeted to a specific antigen known as CD 30, which appears in various cancers including acute myeloid leukemia (AML) and myelodysplastic syndromes (MDS).

SGN-35. This is a strong one. SGN 35 is an ADC.

The mAb is linked to Genentech's drug Auristatin. Testing is now in Phase I for blood-borne malignancies including Hodgkin's lymphoma.

SGN-30. This antibody is targeted to the cancer antigen CD30.

Seattle Genetics has National Cancer Institute sponsored clinical trials ongoing to test in combination with chemotherapy.

The tests are on Hodgkin's lymphoma and anaplastic large-cell lymphoma (ACL).

SGN-70. An exciting development that could rock biochemistry. Its target is renal (kidney) cancer as well as nasopharyngeal cancer and some blood cancers.

Its target is specifically the antigen associated with those conditions that is known as CD70. This antigen is expressed in the T-cells and B-cells of those cancers when active, but not when at rest.

This means that SGN-70 may be of help in treating autoimmune diseases eventually

SGN-75. This one is an ADVC linking the engineered antibody to an Auristatin derivative.

It is hoped that SGN-75 will have value for treating renal cell cancer,

some blood malignancies and some autoimmune diseases.

Seattle Gen Has Important Friends—With Money

Startup biotechs can run losses for years, staying alive only as long as some investors think that someday they will get a drug to market.

It's one of the biggest worries early-stage biotech investors must face. Fortunately, Seattle Genetics is far safer than most on that score.

Its therapies are so well regarded that other companies have been generous in backing them.

Millennium committed to about \$75 million over three years for the development of Brentuximab Vedotin.

If the drug goes to market, Seattle will have rights to U.S. and Canadian sales and Millennium would have the right to commercialize it in the rest of the world.

Seattle would receive royalties on those sales.

This is typical of its agreements. So far, Seattle Genetics has research and development and collaboration funding agreements with these notable partners:

- Millennium
- Bayer
- GlaxoSmithKline
- Daiichi Sankyo
- Progenics
- MedImmune
- Celldex
- Genentech

Already On Board... Those Who Know

I first recommended Seattle Genetics in March 2008. As a last step, I looked at insider activity to see what was what.

Seattle Genetics “smart-money” early investors were very smart money.

The Bill and Melinda Gates Foundation sprang for 5% of Seattle Genetics’ shares/ And though the Gates may be hometown buddies, they paid up for the privilege, buying in at over \$11 a share.

Ned Johnson was another early backer. That name eludes you? He

happens to be chairman of FMR Corp. But even more famously, for the last three decades he has been chief of the family business—Fidelity Investments.

But the insider buying that is most intriguing is the enthusiastic buying from a group called Baker Brothers.

Meet Your New Best Friends

Those Baker boys are something special.

There are two of them. Felix is the scientist with the pertinent background. He got his Ph.D. from Stanford in immunology. Julian got his bachelor’s from Harvard. In Social Studies. Together, Felix and Julian run Baker Brothers LLC and three other related private investment funds that specialize in biotechs.

And they’ve got the hot hand. At just the right times, they have backed Biocryst, Incyte, ViroPharma, Idera Pharmaceuticals, Genomic Health and Alios Therapeutics. All became winners.

Three of those have already made over 100% within months.

Their record goes so far beyond chance, beyond mere superior performance, that it's stunning. Biotechs have dozens of losers.

It's almost impossible to miss them among the small new companies because of the FDA hurdles in their way and the money it takes to support them through years of experimentation and testing.

And these investors have taken a piece of Seattle Genetics in all four funds they manage.

At over \$11 a share. Not only that, when the market dragged all stocks this past year, they went back in and loaded up again.

The One to Buy for the Next 20 Years

This is a company you should own now.

In the coming year, Seattle Genetics story is bound to reach more ears. With one of its drugs already in Phase III trials and on the verge of a potential new drug approval, Seattle Genetics will become much more

visible and much more appealing to investors who are not so adventurous.

The stock should explode when that happens.

Buy **Seattle Genetics (SGEN)** now.

This will be one to brag about.

