**Breast Cancer News: Geron Drug Fails, Herceptin® May Increase Heart Problems, Sunshine Biopharma Heading for Clinical Trials**

Nobody said developing a new cancer drug was easy. Geron Corp. (NASDAQ: GERN) shares took a nosedive last Monday, falling more than 50 percent as the drug maker disclosed that it is discontinuing a randomized Phase II clinical trial of its anti-cancer drug Imetelstat in metastatic HER2-negative breast cancer patients. Menlo Park, California-based Geron said that the median progression-free survival in the Imetelstat arm was shorter than in the comparator arm in the trial. Imetelstat was being evaluated in combination with paclitaxel, compared to paclitaxel alone.

Worse yet, Geron said that things aren’t looking good for Imetelstat hitting its primary endpoint in a study against non-small cell lung cancer (NSCLC) either, although the Phase II trial will still continue. An interim analysis of the study suggests only a modest trend of efficacy in favor of the Imetelstat arm as compared to controls. The outlook at this point is not bright for advancement of Imetelstat to the pivotal third stage of clinical trials against NSCLC.

The news also had a collateral negative effect because Geron had abandoned its leadership position in stem cell research to focus on cancer studies less than one year ago.

The silver lining for Geron shareholders is that Imetelstat still has potential. It is also under evaluation in two hematologic malignancies: multiple myeloma and essential thrombocythemia. The company anticipates releasing top-line results from these studies in the fourth quarter of this year. Geron also has GRN1005 which is currently in phase II studies for brain metastases arising from non-small cell lung cancer and breast cancer. Interim data from the GRN1005 breast cancer trial is expected in early December. Positive data there could provide resurgence in share value.

It is also noteworthy that the company – which is now valued at $174.5 million after the Monday plunge – still has $122 million in cash and investments on hand as of the end of the second quarter. This certainly can wend way for speculation that the firm is now undervalued with its drugs still in development.

Also in the news recently was a new study by the Group Health Research Institute in Seattle which determined that Herceptin® (trastuzumab), the monoclonal antibody that interferes with the HER2/neu receptor from Swiss drug maker Roche Holding AG (OTCQX: RHHBY), increases the risks for heart problems in breast cancer patients significantly more than originally thought. Used either alone or in combination with chemotherapy, Herceptin® is one of the most widely used drugs in the world to combat breast cancer.

Roche, the world’s biggest cancer drug manufacturer, relies heavily on Herceptin® as its third largest drug in sales annually. Herceptin® sales tallied $5.5 billion last year. Sales in the first half of 2012 have risen to about $3 billion. The big biotech is expecting results from 19 clinical trials in the next 18 months to offset any potential decrease in sales of Herceptin® as it faces its latest hurdle and patent expiration in 2014. Twelve of its 19 late-stage trials involve new drugs for a variety of indications.

In November 2011, the FDA revoked the approval of Roche’s Avastin® (bevacizumab) as a treatment for breast cancer, but it still retained its indications for colon, kidney, lung and brain cancer.

Erin Aiello Bowles, an epidemiologist at the Group Health Research Institute and lead author of the study published in the Journal of the National Cancer Institute, explained that the data collected in clinical trials excluded many women that receive the treatment in the real world. The women, generally older or with a pre-existing conditions, were not allowed to be part of the clinical trials.

Bowles’ study, which examined 12,500 women diagnosed with breast cancer, found that the overall risks of developing heart failure or cardiomyopathy when trastuzumab was taken alone are greater than chemotherapy alone. As a combination therapy with chemo, the risks proved to be even greater than trastuzumab as a stand-alone treatment.

“These drugs are toxic. They kill cancer cells, and sometimes kill other cells in the body, too,” commented Bowles. Not discounting the efficacy, though, Bowles continued, “These drugs are still important for women with breast cancer to use because we know they improve survival. But as with any drug, people need to be aware of the risks, too.”

Bowles also explained that the risks were also correlated to age, with elderly patients experiencing a greater likelihood of serious heart complications.

Education could also be a driving force to help fight subsequent long-term side effects. According to the American Cancer Society estimates, there are more than 12 million cancer survivors alive in the United States. The problem lies in secondary battles with life-threatening effects from cancer treatments. Recent data from a June meeting at [The American Society of Clinical Oncology](http://www.msnbc.msn.com/id/47697249/ns/health-cancer/t/cancer-survivors-face-new-test-long-term-care/#__utma=14933801.889352190.1343650043.1346859667.1347535647.8&__utmb=14933801.1.10.1347535647&__utmc=14933801&__utmx=-&__utmz=14933801.1347535647.8.2.utmcsr=google|utmccn=%28organic%29|utmcmd=organic|utmctr=%28not%20provided%29&__utmv=14933801.|8=Earned%20) showed that 94 percent of primary care doctors are unaware of the potential long-term effects of commonly used drugs to treat breast and prostate cancer.

Geron and Roche have been focused on HER2 (human epidermal growth factor receptor 2). The HER2 gene makes HER2 proteins, receptors on breast cells that normally help control how a healthy breast cell grows, divides, and repairs itself. But in about 25 percent of breast cancers, the HER2 gene is dysfunctional and makes too many copies of itself which leads to breast cells growing and dividing in an uncontrollable fashion.

The other gene commonly associated with aggressive forms of breast cancer is TOP2 (Topoisomerase II). TOP2 enzymes are critical in transcription, replication and chromosome segregation which has made them a topic for anti-cancer drugs, but the pathway has been somewhat elusive to date. TOP2 is also an important target for many other cancer lines in addition to breast cancer, including prostate, colon, lung, stomach and ovarian. Currently, the drug of choice targeting TOP2 in cancer patients is etoposide; marketed as Etomedac®/Eposin by Medac and by Bristol Meyer Squibb (NYSE: BMY) as Etopophos® and Vepesid®.

Looking to move down the regulatory pathway focused on TOP2 in breast cancer patients is Sunshine Biopharma (OTCBB: SBFM) with its Adva-27a drug candidate. Published laboratory data show that Adva-27a is a true TOP2 inhibitor and is significantly more effective at killing multidrug-resistant breast cancer cells (MCF-7/MDR) and small-cell lung cancer cells (H69AR) than etoposide.

Sunshine has taken delivery from the Contract Manufacturing Organization (CMO) and is now conducting a series of requisite biological tests to ensure that the newly manufactured batch is identical to the original, not only in terms of chemical structure but also in terms of biological activity. The company plans to initiate Phase I clinical trials for Adva-27a in 2013 at the Jewish General Hospital, Montreal, Canada, one of McGill University's Hospital Centers.

The American Cancer Society estimates that in the United States there will be about 230,000 new cases of breast cancer diagnosed in 2012 and about 40,000 deaths from the disease. Roche’s Herceptin® may be facing some obstacles in the near term and the patent cliff in 2014, but sales have been steadily increasing since its 2006 FDA approval. Notably, the drug only targets about 15 to 20 percent of breast cancer patients. Gauging potential market value for Sunshine’s Adva-27a from Roche’s sales of Herceptin, it is discernible that its market capture could be far greater being that the TOP2-positive breast cancer patient population is much larger.