

## **GSK's Allan Roses Says PGx Is Not Only Here, It's Already Paying Off**

*By Bernadette Toner, editor, BioInform*

BOSTON, April 6 (GenomeWeb News) - The era of pharmacogenomics has officially begun, according to Allan Roses, senior vice president of genetics research at GlaxoSmithKline, who showed examples of how his company is seeing clear benefits from the application of genomic tools in its discovery and development pipeline.

Speaking yesterday at the Bio-IT World Life Sciences Conference and Expo here, Roses said he wanted to "attack the notion that personalized medicine and pharmacogenomics are years away." As evidence, he presented a number of examples in which GSK has already seen a clear payoff from the approach.

One of those examples was the company's announcement earlier this week that had halted patient enrollment for a phase III clinical trial combining its breast cancer drug Tykerb (lapatinib) and Xeloda (capecitabine) versus capecitabine alone because the efficacy of the combination therapy exceeded its primary endpoint of time to disease progression.

GSK relied on pharmacogenetics to identify patient populations likely to respond to Tykerb --- a strategy that should help the company shorten its time to market.

Roses explained that in a previous study with the cancer drug, around 15 percent of 107 patients experienced diarrhea and skin rash, but GSK performed association studies with five genes and determined that only those patients with a CYP2C19 mutation exhibited those adverse events. Furthermore, three out of four patients who withdrew from the trial because their side effects were more severe were found to be homozygous for the CYP2C19 mutation.

Armed with that information, GSK knew that it should lower the dosage of the drug for those patients with the mutation, which led directly to the shortened timeline for the phase III trial.

"That's what pharmacogenetics can do," Roses said.

Roses also discussed how GSK is using genetic profiles to define clinically responsive patients in a phase IIA study for an obesity drug and in a phase IIB study for a diabetes drug with potential indications in Alzheimer's disease.

Roses said that GSK has fully embraced pharmacogenomics as part of its drug-development process. The company currently requires informed consent for DNA collection in all of its phase I, II, and III studies, and plans to extend that strategy to phase IV this year, he said.

GSK has also begun "selective" collection of plasma, serum, and urine samples, along with imaging data, to help it identify "endo-phenotypes" in longitudinal biomarker studies, and has committed to "identifying pharmacogenomics opportunities in every clinical study," Roses said.

In addition, the company has just begun performing genome-wide screens under its HiTDIP (high-throughput human disease-specific target program) using the Affymetrix 500K chips with the aim of finding genetic disease associations for a broad range of diseases, beginning with Alzheimer's and obesity.

Roses said that GSK plans to publish each disease study it performs, and that it will release the data from those studies into the public domain.