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Glaxo Shows Aequorin Superior to FLIPR; Shifts to Luminescence for HTP Imaging

[SAN DIEGO] – **FOLLOWING AN 18-MONTH** trial, researchers at GlaxoSmithKline this month began transitioning from fluorescence imaging to luminescence imaging for high-throughput calcium-mobilization assays done in the 1,536-well format, a company official said during a recent conference.

Speaking at a session on assays and screening advances at the Assays and Cellular Targets meeting here this week, Parita Shah, team leader for screening and compound profiling at Glaxo, said the benefits of using aequorin for high-throughput calcium mobilization assays include better data quality, reduced cycle time and cost, and the ability to schedule assays “on the fly” within 24 hours of plating the cells.

“Now any new assays that come in will go directly to the aequorin format,” Shah told CBA News on the sidelines of the conference, adding that Glaxo will still run

fluorescence assays with GPCR and ion channel and membrane potential assays.

When her team used aequorin and PerkinElmer’s LumiLux reader for structure-activity relationship assays and compared their results to those from fluorescence imaging done on MDS Analytic Technologies’ Fluorometric Imaging Plate Reader platform, they found fewer plate failures due to variability (42 percent versus 0) and fewer rejected AutoCurve fits (13 percent versus less than 0.1 percent).

When Shah and her team ran two HTS campaigns in parallel on FLIPR and

aequorin, they found that the aequorin assay required two fewer employees, had a five-plate-per-hour higher throughput, and confirmed 55 percent more single-shot actives at XC50 compared to FLIPR. In addition, FLIPR had a 6.5-percent-higher plate failure rate than aequorin.

Although the initial assay optimization went well, the researchers needed to extend the trial by two months to understand and resolve issues concerning tip loading and washing, Shah said.

She also said that aequorin can be used to drive structural activity relationships in both agonist and antagonist programs; it yields better reproducibility and plate-failure rates compared to fluorescence; it requires 75-percent less time than fluorescence to complete an HTS campaign; it reduces manpower requirements; and it cuts cell-culture

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requirements in half compared to fluorescence.

Shah said she anticipated these improvements because “that was something we were hoping to see. Quite often when you run these trials, you think that you are going to have all of these benefits, and then you end up seeing none at all.”

Additional benefits to aequorin include a more timely response to screening requests because cell culture plates do not have to be plated 24 hours in advance, and the ability to spend the manpower saved on more value-added assays, such as native tissue assays, Shah said.

“I think in the HTS area ... the industry is transition-

ing to aequorin, namely those who want to miniaturize to 1,536 wells,” she added. Glaxo’s compound library is becoming more extensive and drug discovery is moving at an overall faster pace, she said.

Glaxo started with a trial that lasted several months and looked at a whole range of different receptors, because the company and its customers had to be convinced that it could deliver the same data robustness and show all of the benefits that it was looking for, Shah said.

By Charlotte LoBuono