Qualyst Transporter Solutions Launches the C-DILI™ Assay

A novel *in vitro* model to predict a compound's cholestatic hepatotoxicity risk

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Durham, N.C. (March 10, 2017) – Qualyst Transporter Solutions, LLC (QTS) introduced the C-DILI Assay[i], a novel *in vitro* method to evaluate a compound's potential for cholestatic drug-induced liver injury (DILI). The C-DILI Assay has demonstrated high *in vitro-in vivo* correlation and is an effective tool for lead selection and in managing toxicity risk.

"Current *in vitro* models are poor predictors of clinical cholestatic DILI", said Dr. Kenneth Brouwer, Chief Scientific Officer at QTS. "That is because these models do not account for liver cells' compensatory and regulatory mechanisms in response to stress. In addition, *in vivo* models are inadequate because the livers in species such as rat have a different mix of bile acids and have different metabolism and regulatory mechanisms compared to humans."

At high concentrations, bile acids can cause liver toxicity by signaling apoptotic pathways as well as disrupting membranes. The liver tightly controls bile acid concentrations through multiple regulatory mechanisms including basolateral efflux, biliary efflux, synthesis, and metabolism. However if control mechanisms are disrupted by compounds, bile acid concentrations can reach a "tipping point" resulting in hepatotoxicity. Current *in vitro* models only focus on a few isolated efflux transporters and not the integrated process.

The C-DILI Assay combines all of these human-relevant processes in one simple threshold readout by measuring levels of lactate dehydrogenase (LDH); thus it provides a unique clinically-predictive assessment of cholestasis risk. In the assay, hepatocytes are cultured in conditions that allow evaluation of their response to a test article and the test articles are compared to positive, negative and solvent controls.

"We are pleased to add the C-DILI Assay, a simple "hepatotoxic / not hepatotoxic" evaluation, to our portfolio of products and services. We have shown excellent clinical predictions with the assay in over 50 clinically-described compounds; we truly have something that is next-generation", said Dr. Christopher Black, CEO of QTS. "The assay can be used as a screen early in the process, and the same system, and even the same hepatocytes, can be used to do a deep dive and answer more mechanistic questions later in the process. We believe this is of enormous value to our customers", added Dr. Black.

About Qualyst Transporter Solutions, LLC

Qualyst Transporter Solutions, LLC (QTS) provides *in vitro* hepatic models to predict the effect of drugs and other compounds on the human liver. QTS' *in vitro* models integrate hepatic uptake, metabolism, regulation, and efflux and demonstrate superior *in vitro-in vivo* correlation compared to conventional systems. QTS' proprietary technology, products, and services are used by leading pharmaceutical, nutrition, cosmetics and consumer products, and chemical companies to provide clinically-relevant answers to liver-related questions, and to address regulatory concerns about their products.

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[i] The C-DILI Assay is a trademark of Qualyst Transporter Solutions, LLC