Safety issues account for about a quarter of the attrition in drug projects. If it is a result of the primary pharmacology, you have to either drop the target entirely or manage the risk. However, if this arises from off-target activity, you have the additional option to dial this out and avoid the associated adverse events (AEs). This is the discipline of Secondary Pharmacology, the focus of Certara’s new in silico technology.

SECONDARY INTELLIGENCE: PREDICTIVE TECHNOLOGY FOR IMPROVING SAFETY PROFILES

Secondary Intelligence™ assembles, curates and visualizes all secondary pharmacology analyses, providing key information on potential AEs, quantitatively rating each compound as to its likelihood of causing off-target safety issues that could impact clinical progress. The first module in Certara’s ToxStudio™ integrated modelling & simulation platform for safety pharmacology, toxicology and patient safety, Secondary Intelligence™ is the only tool available to address this translational challenge.

- Secondary Intelligence assembles curated, organised information for a compound’s secondary pharmacology readouts and analysis in one place.
- It provides up-to-date literature-based information on the expected side effects of a given compound as it engages with a particular off-target receptor in clinical use.
- This data enables virtual in vitro in vivo extrapolation (IVIVE).
- It rates each compound with a ‘low’, ‘intermediate’ or ‘high’ likelihood of causing AEs at the off-target receptor in clinical use, based on quantitative analysis of clinically used drugs that specifically target that receptor, and on its predicted plasma Cmax.

Like radar, Secondary Pharmacology provides early alerts and allows you to decide on your next move.

For each receptor, we evaluated all the drugs that target it for their therapeutic efficacy, and for which an interaction at this receptor was their primary pharmacological effect.

We detailed their main pharmacodynamic effects and side effects, summarized in a table for each receptor.

That data is what you would expect to happen with your compound in clinical use if its interaction with this receptor was sufficiently high at clinical exposures.

To aid visualization and go/no go decision making, the SW categorizes your test compounds relative to the reference drugs to determine likelihood of causing AE in clinical use.

We collated data on the reported free plasma concentration for eliciting PD effects, collected potency data from in vitro assays and plotted the ratio of the free plasma concentration divided by the Ki (or IC50) for each drug.

We have also constructed a Receptor Liability Pathway for each of the side effects, using the structure of Adverse Outcome Pathways to assess how hard we have to hit that receptor to see those effects.
Secondary Intelligence software identifies the key safety/tox information about each receptor, allowing you to focus on how a test compound interacts with that receptor. It can address safety performance against multiple receptors. Secondary Intelligence ranks the likelihood of each off-target interaction during clinical use, color-coding in red, amber or green.

Secondary Intelligence prioritises “receptor interactions of concern” in a variety of data representations, and ranks compounds against each other to make quantitatively based decisions as to which compounds to progress.

About Certara
Certara accelerates medicines using proprietary biosimulation software, technology and services to transform traditional drug discovery and development. Its clients include more than 2,000 biopharmaceutical companies, academic institutions, and regulatory agencies across 62 countries.

For more information visit www.certara.com or email sales@certara.com.