CERTARA

Secondary Intelligence™

Safety issues account for about a quarter of the attrition in drug projects. If this is caused by the primary pharmacology, you have to either drop the target entirely or manage the risk. However, if this arises from off-target activity, there is the additional option of dialling this out and avoiding 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 uses off-target screening data to quantitatively predict safety outcomes *in vivo* and in the clinic

- 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 if 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 C_{max}.
- Secondary Intelligence will integrate with Certara's Simcyp® PBPK software platform, which is crucial for the assessment of the relevant tissue concentrations.

For each receptor, we evaluated 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 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.

We have also constructed a Mechanistic Safety Pathway for each of the side effects, using the format of Adverse Outcome Pathways.

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.

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

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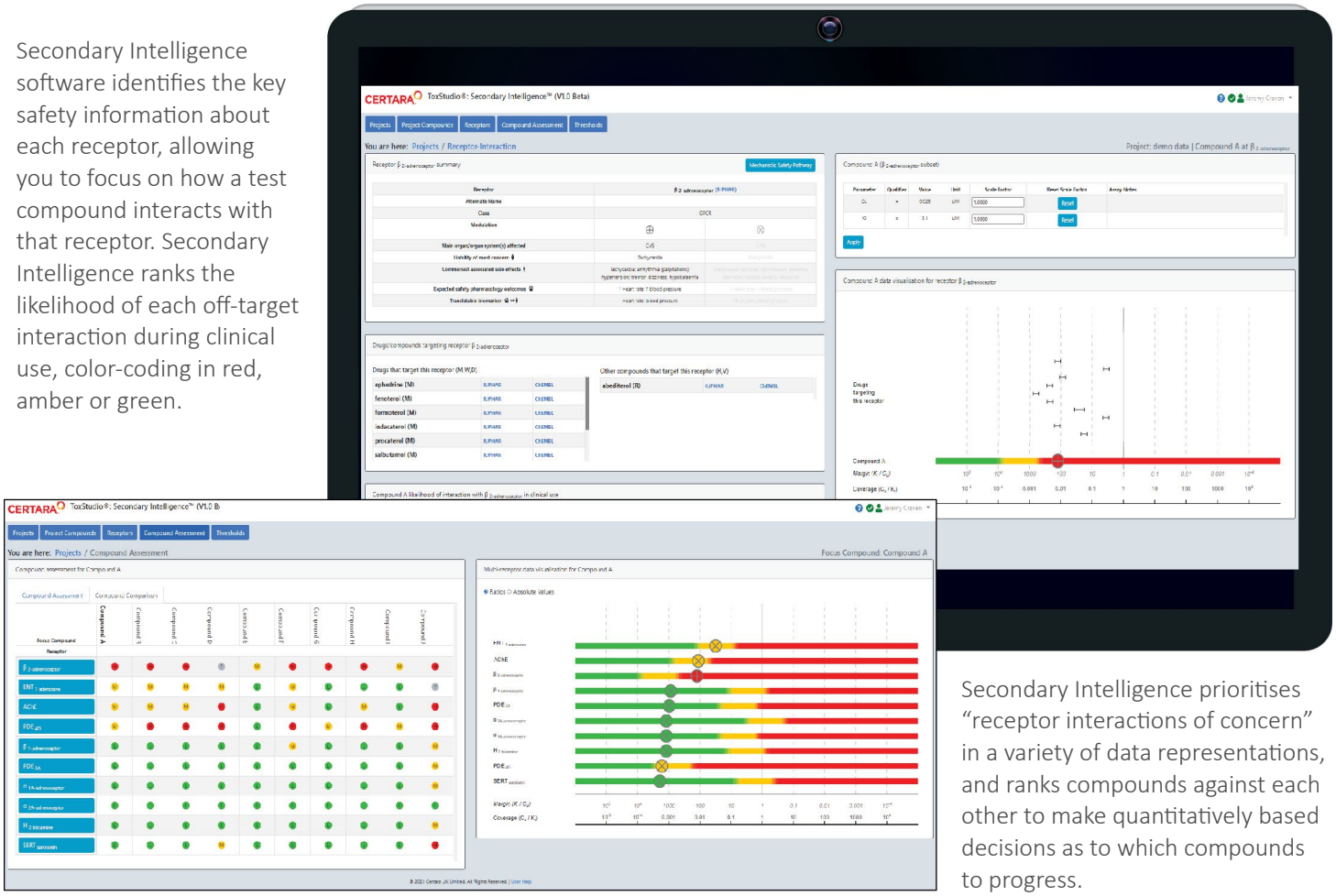
Secondary Intelligence from Certara: Secondary Pharmacology re-imagined.

Secondary Intelligence software identifies the key safety information about each receptor, allowing you to focus on how a test compound interacts with that receptor. 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 optimizes R&D productivity, commercial value and patient outcomes through its unique portfolio of model-informed drug development, regulatory science, and market access solutions. In fact, 90+% of all novel drugs approved by the US FDA in the past six years were supported by Certara software or services. Its clients include 1,600 global biopharmaceutical companies, leading academic institutions, and key regulatory agencies across 60 countries.

For more information, visit **www.certara.com**.