Agentic orchestration of drug discovery ML tools under partial observability

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1. Ignota Labs

TLDR; We present a prototype that coordinates heterogeneous predictive models under uncertainty and partial observability that provides an agent driven reasoning for drug turnaround

1. Background

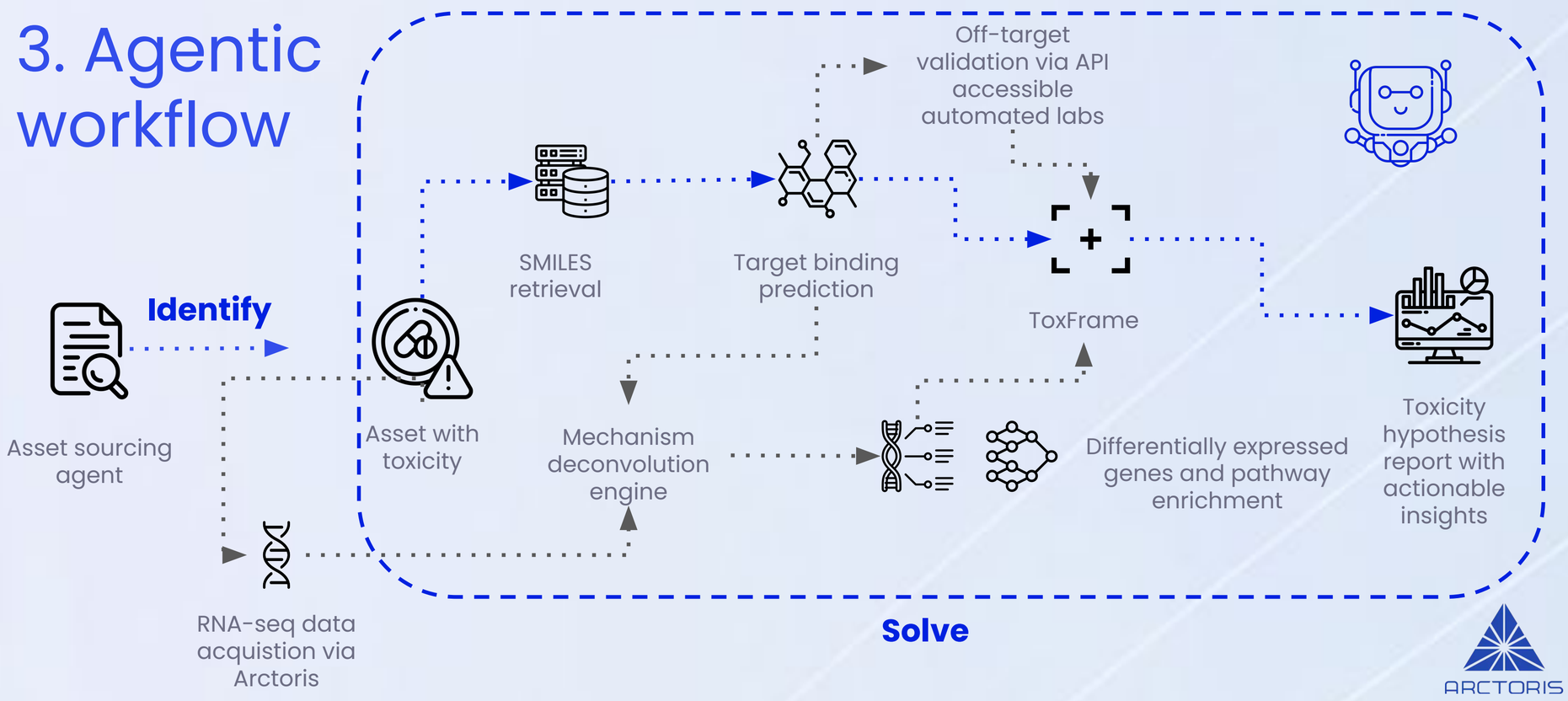
Off-target toxicity is a leading cause of drug attrition from the clinic. Machine learning, bioinformatics, and cheminformatics approaches allow for more granular modelling of compound behavior such as off-target interactions and pathway perturbation[1]. These tools allow learnings from many scientific data sources. To manage an increasing volume of internal leads; we are utilising these tools via an orchestrating agent to save failed drugs by identifying and solving the associated toxicity and bringing these drugs back to the clinic.

2. Tools

Ignota Labs have four in-house tools which are utilised within this agent:

- Asset sourcing agent, which integrates patents and commercial datasets to identify failed assets
- Target binding prediction over the entire human proteome
- Mechanistic understanding, through RNA-seq analysis and pathway deconvolution[2]
- ToxFrame, contextualisation of predicted off-targets and observed toxicities for hypothesis generation

3. Agentic workflow

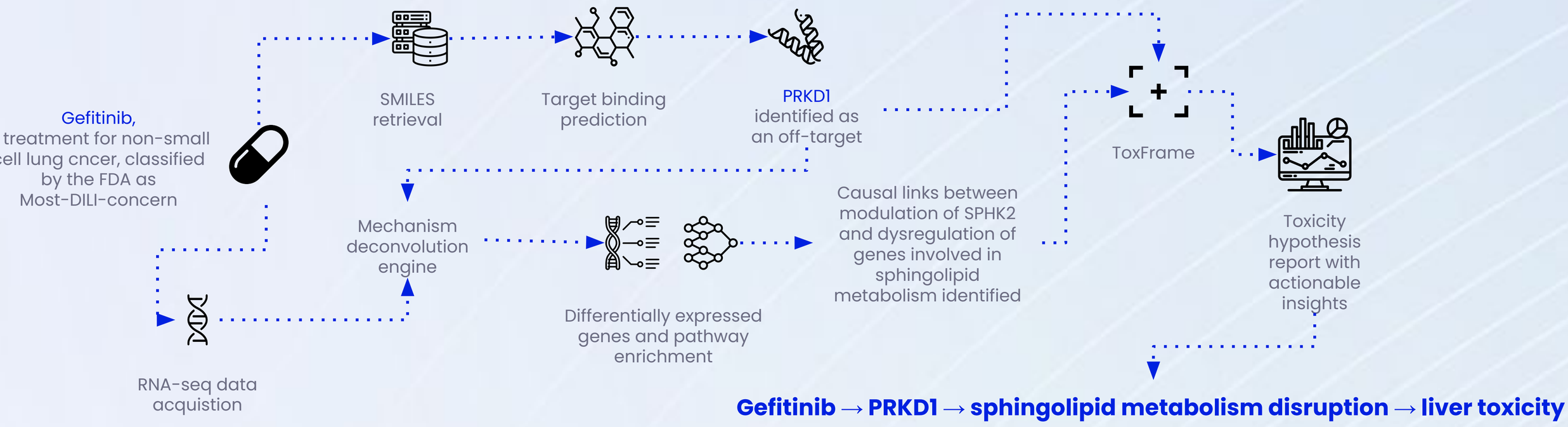


Our orchestrating agent has access to the tools described above, by identifying the relevant available data it can generate a toxicity hypothesis report based on the data and associated literature.

Our lab-in-the-loop partner, Arctoris, provide integratable experimental protocols, providing speed, efficiency and agentic decisions to be injected into our experimental workflow.

4. Preliminary case studies

Two case studies have been carried out for assets which cause Drug Induced Liver Injury (DILI); Gefitinib[3] and Ketoconazole.



Our agent was able to draw conclusions on the cause of hepatoxicity for Gefinitinb, drawing novel conclusions for the reasons for toxicity behind the previously identified PRKD1 off-target. By combining cheminformatics, bioinformatics and our literature reasoning agent we have drawn novel conclusions around the underlying mechanism of toxicity for Gefitinib.

References

1. Masarone S, Beckwith KV, Wilkinson MR, Tuli S, Lane A, Windsor S, Lane J, Hosseini-Gerami L. Advancing predictive toxicology: overcoming hurdles and shaping the future. Digital Discovery. 2025;4(2):303-15.
2. Hosseini-Gerami L, Lane J, Masarone S, Wilkinson M, Windsor S. P05-44 SAFEPATH: Using AI to understand the molecular mechanisms causing safety failures, enabling drug optimisation and turnaround. Toxicology Letters. 2024 Sep;399:S149-.
3. Hosseini-Gerami L, Masarone S, Lane J. Using SAFEPATH to Uncover a Novel Mechanism of Hepatotoxicity for Gefitinib. bioRxiv. 2024 Jul 31:2024-07.

Paper link

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