Case Study

30 alternate indications identified for six shelved compounds

The Purpose

A large pharma company was looking to expand its portfolio for six shelved assets (four failed in clinical development Phase II & III and two at the preclinical stage) using drug repurposing.

About the Client

INDUSTRY
Pharma

LOCATION
US

THERAPEUTIC AREA
Multiple

Client Requirement

The partner was interested in identifying alternate indications for their assets by an integrated strategy. The objective was to combine in silico analysis through Excelra's proprietary platform with validation through wet lab experiments. Indications corroborated through these two independent workflows would be prioritized.

The Excelra Approach

The six compounds were analyzed with a comprehensive in silico pipeline. This includes Excelra's proprietary repurposing platform, 'GRIP' to generate a biological rationale for its use in new indications. Further, validation was conducted using a Multi-OMICS approach, conducted in a wet lab to provide a final list of indications per compound.

Solution Strategy

In silico analysis

Omics analysis

Correlation of both
in silico and omics analysis

Overview of In-silico Analysis

Excelra's novel and proprietary repurposing platform GRIP (Global Repurposing Integrated Platform) allows for an integrated approach by leveraging the following core components:

GRIP - The customized Global Repurposing Integrated Database is a compendium of 40+ public & proprietary databases and creates multi-dimensional profiles of biologically relevant entities such as genes, pathways, biomarkers and adverse events
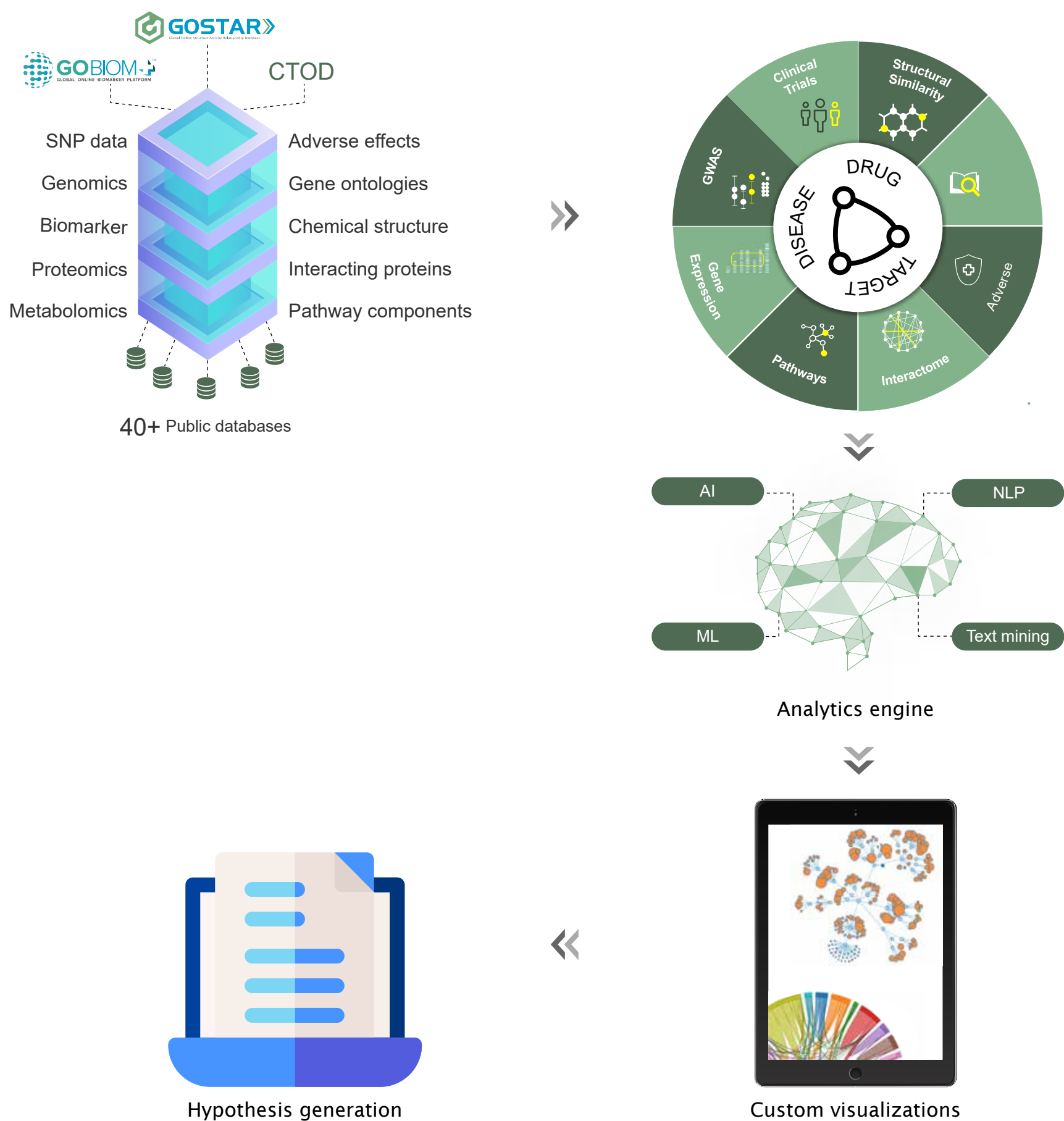
The Holy Trinity - 3-way relationships established between drug, disease and target that help understand relevant associations

Algorithms - Customized proprietary algorithms which have been developed internally to mine the drug-target-disease associations from GRID

Analytics & Visualization - In-house analytical capabilities and visualization tools that enable identification of hitherto hidden connections between drugs, disease and targets

GOSTAR
GOBIOM **CTOD**

SNP data	Adverse effects
Genomics	Gene ontologies
Biomarker	Chemical structure
Proteomics	Interacting proteins
Metabolomics	Pathway components

40+ Public databases

DISEASE • DRUG • TARGET

Clinical Trials • Structural Similarity • GWAS • Adverse • Gene Expression • Pathways • Interactome

AI · NLP · ML · Text mining

Analytics engine

Custom visualizations

Hypothesis generation

Drug-disease-target associations Biological insights Testable hypothesis Disease models for PoC

Overview of Omics Analysis

Excelra's capabilities in handling OMICs data range across multiple data archetypes. In this engagement, the clients shared drug-treated in vitro & in vivo genomics and metabolomics data for the asset based on the recommendations from the previous in-silico analysis. The multi-OMICs analysis approach used here consisted of analyzing that data to further validate the shortlisted alternate indications that could be recommended to the clients.

The results from the multi-omics analysis were then used to corroborate the in-silico analysis to state the final recommendations, with all the supporting biological rationale in place to validate the final outcomes.

01 Experimental design → **02** In vitro/in vivo experiments → **03** Data generation → **04** Data analysis
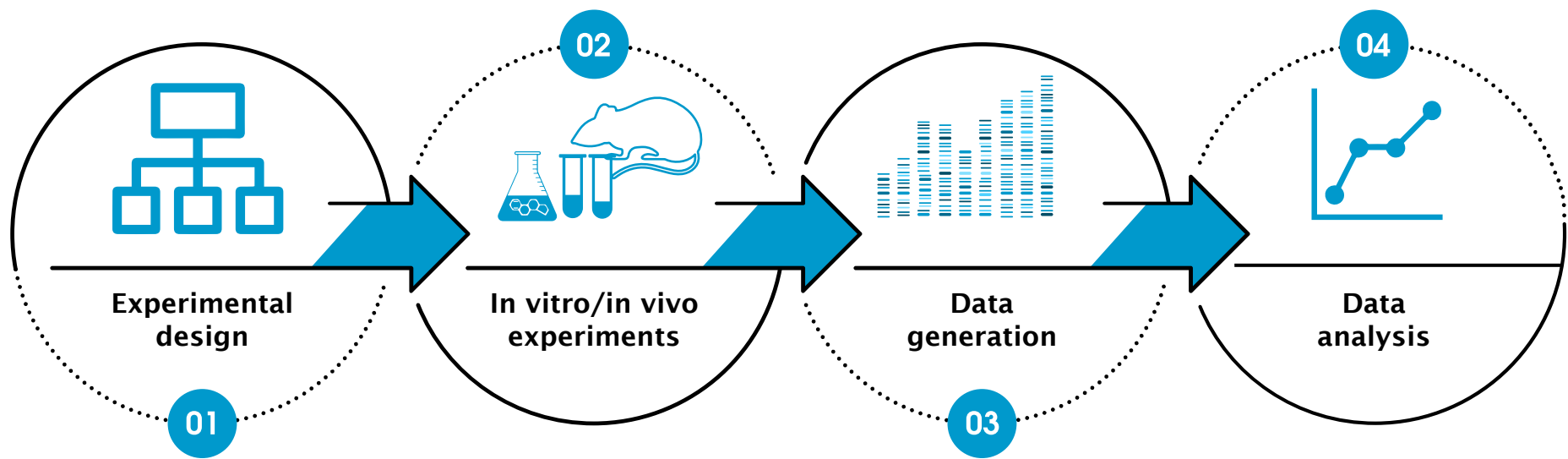
Excelra's Contribution

The combined in-silico and multi-omics analyses helped expand the client's portfolio by leveraging data-driven approaches corroborated with wet lab validation, ultimately leading to robust recommendations.

Some key highlights from the outcomes are:

Alternate indications for the six compounds were identified in silico and validated in vitro/in vivo. One of those compounds progressed to IND filing

For a compound shelved during preclinical development for the gastrointestinal/autoimmune disorder was repositioned for Alzheimer's disease

A compound for which the Target/Mechanism of Action was previously unknown, was repurposed for a new indication using lipidomics data

For a compound discontinued in clinical development due to hepatotoxicity, an alternate use of diseases requiring topical administration was identified

Excelra's Service Portfolio

	Insights	Data
Discovery	• Data Science Driven Drug Discovery • Target Identification • Target Dossier Services	• Chemistry Curation Services • **GOSTAR** *Structure Activity Relationship database*
Translational	• Biomarker Discovery • Drug Repositioning • Life Cycle Management • Systems Biology Informatics	• Biology Curation Services • **GOBIOM** *Biomarker intelligence database*
Clinical	• Precision Oncology Informatics • Clinical Pharmacology	• Clinical Trial Outcomes Database
Value Evidence	• Outcomes Research • Epidemiology Modelling • Economic Modelling • Value Evidence Communication	• RWE & Big Data Realization • SLR & Meta-Analysis
Technology Solutions	• Enterprise Data Strategy • Enterprise Cloud Ops • Enterprise Digital Transformation	

For more information, visit https://www.excelra.com/translational/#drug_repositioning

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About Excelra

Excelra's data and analytics solutions empower innovation in life sciences from molecule to market. The Excelra Edge comes from harmonizing heterogeneous data sets, applying innovative bioinformatics know-how and technologies to accelerate drug discovery & development with reliable and result-oriented insights.

✉ marketing@excelra.com