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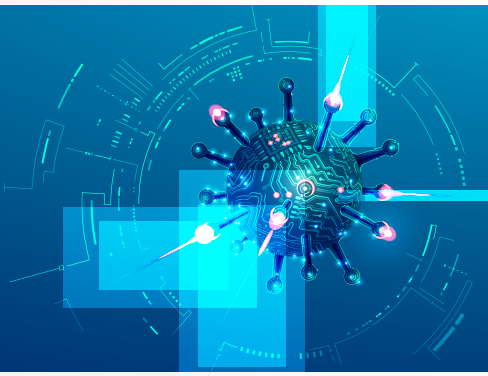
Where data means more

CASE STUDY

Data driven disease-indication expansion and prioritization for specific target inhibitor



Client's Challenge and Goal

Client is a mid-sized biopharmaceutical company, active in the neurodegenerative / neuroinflammatory therapeutic area. They were focused on developing next generation inhibitors for a specific tyrosine kinase and had a promising molecule in preclinical stage for a specific neuroinflammatory disease indication. The client wanted to expand the indication profile of the molecule into other neuro-degenerative / inflammatory indications.

Initiating a new preclinical program is a considerable resource and financial commitment that requires careful multifaceted consideration. The client, therefore, wanted an assessment of all neuro-degenerative / inflammatory indications with the purpose of identifying and prioritizing indications that could be most relevantly addressed with their inhibitor molecule. Generating an appropriate dataset from research and clinical studies and using data analytics on it would be a unique approach to address their purpose.

Our Client

Mid-size Pharma based in North America

Our Approach

The client partnered with us due to the unique data driven approach we were providing to identify and prioritize indications. Excelra has an established legacy in dataset generation and a proven track record in building biomarker database by bringing structure to the vast amount of data available, transforming it into valuable and actionable insights. Having knowledge of the target protein and pathways / biomarkers impacted by the client's molecule, allowed us to build a tailored target centric solution to address the client's requirement. Further, the insights from our approach are driven by data-based quantifications and analytics involving minimal manual assessment. The delivery of the dataset for biomarker-disease landscape along with a data navigation tool adds value to the analysis which the client can tap into post completion of the project as well.

Our Proposed Approach

Biomarker landscape
Comprehensive landscape of all diseases, biomarkers, drugs and clinical outcomes from the public domain, databases, published articles, drug labels and clinical guidelines via text mining, curation followed by building analytics and insights

Target Centric
Focus on Identifying linked diseases, drugs and biomarkers taking target as input

Disease Centric
Starting from prioritized disease and building a complete biomarker landscape

Drug Centric
Biomarker assessment for same target drugs and SoC drugs for prioritized disease

Target Centric Approach

1. Unbiased mapping of all indications connected to target protein pathway
2. Indication prioritization using quantified strength of association to target pathway markers.

Factors contributing to indication scoring & prioritization

Unbiased mapping of all indications connected to target protein pathway

- Number of unique pathway biomarkers linked to a disease
- Evidence of connection- number of studies, type and sample size of study
- Direction of connection- Positive/ Negative
- Specificity of association of biomarker

Deliverable

Biomarker data asset
Structured dataset of all information extracted for biomarkers identified along-with drug-disease associations, clinical endpoints, associated reference ID, synonyms etc

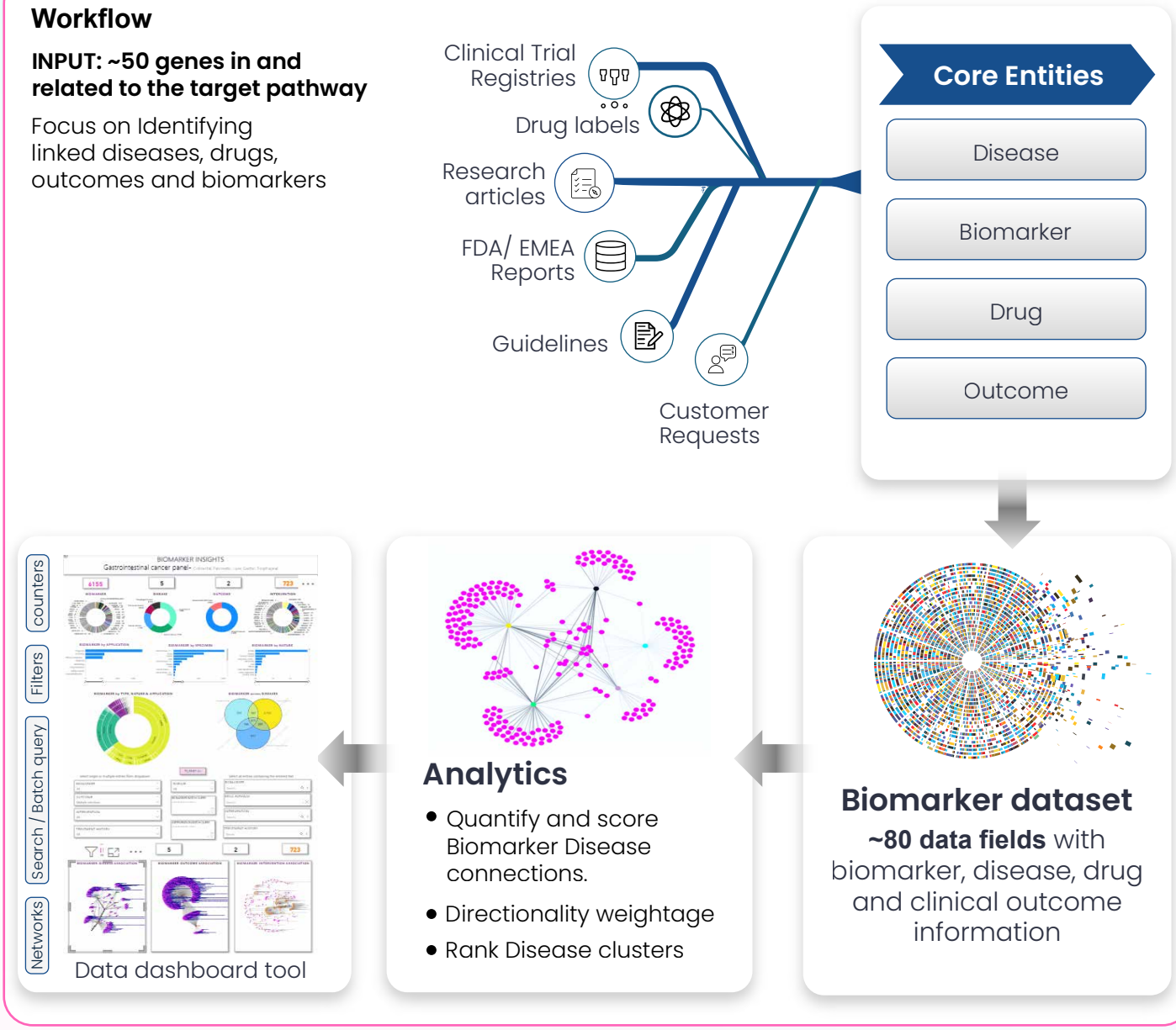
Networks and visualizations
Custom dashboard proprietary to the client. Easy data navigation through visual networks of target-disease-biomarker-outcomes

Our Solution

Workflow

INPUT: ~50 genes in and related to the target pathway

Focus on Identifying linked diseases, drugs, outcomes and biomarkers



Project scope & deliverables: Scope of the project was clearly defined, outlining the specific objectives, data sources and deliverables to ensure alignment with the client's needs. Data delivery was in the form of Excel and a data navigation dashboard with interaction networks between biomarkers, disease, clinical outcome and intervention.

Identification & Screening of relevant articles: Based on the drug target defined by the client, genes of the primary and secondary pathways were listed and used to identify all articles of potential relevance. These were screened and selected as per the defined scope of the study.

Creation of a dataset: To streamline the data curation process, we have developed a structured data extraction template with close to 80 unique data fields. This template contains primary and associated fields to capture all relevant information around the four core entities of the dataset- Biomarker, Disease, Clinical outcome and Intervention.

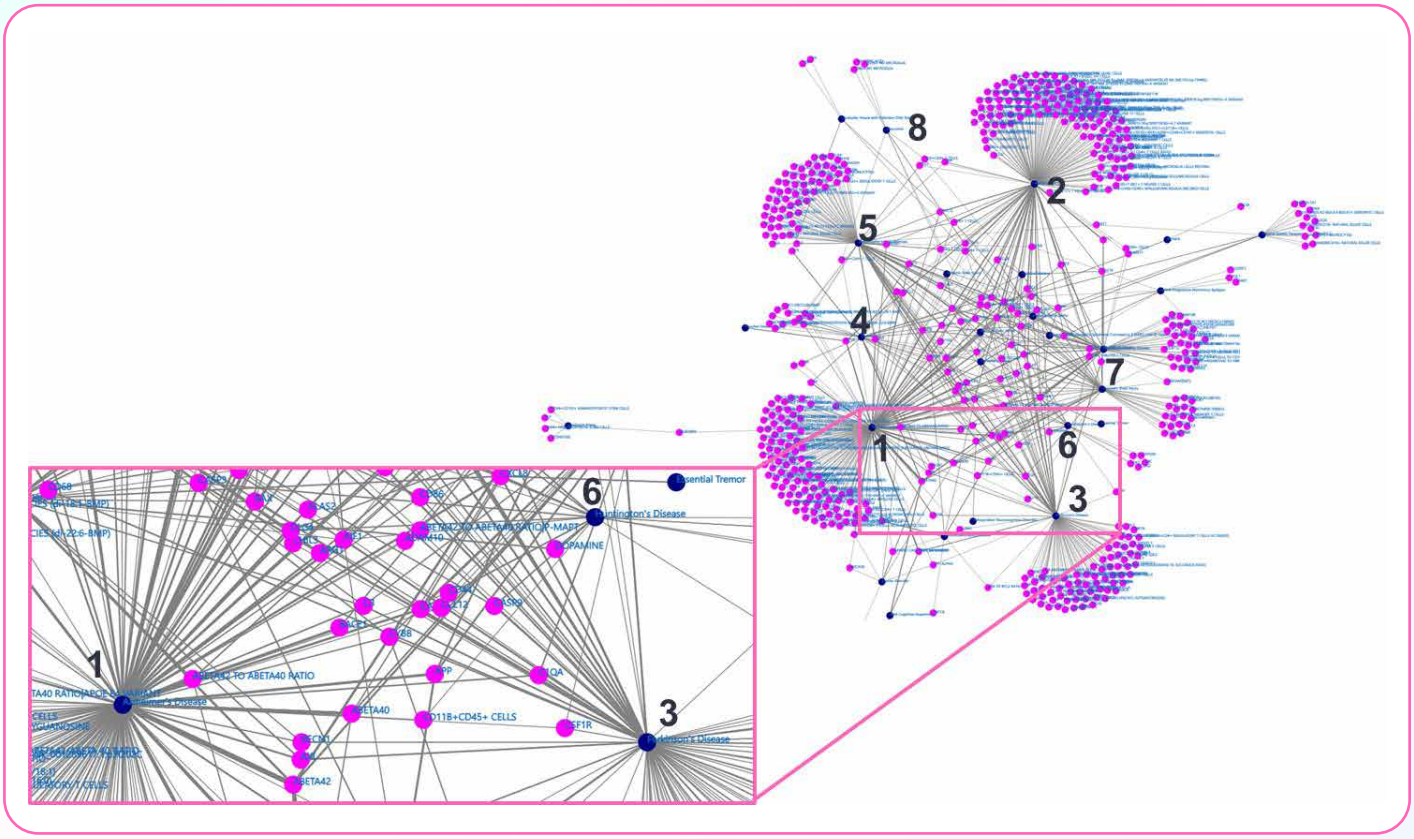
Analytics & Dashboard: To address the client requirement specific scores and weightages are attached to biomarkers and associated fields linking them to each disease (see target centric approach above). This quantification metric is analysed in summation to yield a **disease priority score** specific to the target pathway defined by the client.

A rich dataset was generated starting with the client specific target pathway. Following are some of the top level statistics of the dataset:

484 Articles curated	**150,000** Rows of curated data	**1978** Unique biomarkers
713 mRNA	**629** Protein	**351** Cellular
153 Genetic variants	**45** Neurodegenrative / neuroinflammatory disease indications	**748** Unique clinical outcomes
353 Unique interventions in in *vitro* / in *vivo* / patient studies		

Analytics and quantified scoring lead to prioritization of the 45 disease indications. The information was provided to the client both as a table with top 20 disease indications in order of disease-target relevance score as well as an interactive network visualization where associations between biomarkers, disease, outcomes and interventions could be explored further.

In the image below: Disease (blue nodes)-biomarker (pink nodes) network visualization, the biomarkers link and cluster around disease indications. Connection edge is weighted based on the strength and direction of the link. Selection of genes / biomarkers of a specific pathway alters the network providing insight on most relevant disease indications.



Pathway specific query drives the disease priority order (#1-8). Target pathway shows enrichment in Disease 4 even though the number of linked biomarkers are low as compared to Disease 5.

The disease indication prioritization allows the client to get a list of relevant disease that would make most sense, in context to their target inhibitor. It opens up the opportunity to make an informed decision to pursue further programs with the molecule and increase its potential.

The data driven approach taken by us ensures no manual bias to be introduced into the assessment. The visualization tool allows the client to continue to explore the data further, and include the visuals in presentations for internal use.

Conclusion

The success of this project can be attributed to several key factors. Firstly, Excelra has several years of experience in building biomarker database. Customizing these datasets for a client specific requirement is a natural extension and an established use case of our in-house expertise. Secondly, availability of over a million data points allows scoring, quantifications and data driven insights to emerge, often unexpected but backed by relevant proof.

Further, the Disease-Biomarker landscaping maps all diseases linked to a target, several of them rare diseases with limited patient level or 'omics evidence. Ownership of a visualization/network tool supports continued exploration and further decisions of the client in devising biomarker strategy

A natural extension to such a use case is the construction of a disease-biomarker-drug landscape which supports the drug development program into preclinical and clinical translation. This begins with selection of the top 3-5 of the prioritized indications and an extensive capture of all drugs, response, safety, risk biomarkers and clinical outcomes. Such a landscape is focused exclusively on patient studies making the insights more translatable in the clinical.

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