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# Harnessing the Power of Real-World Evidence from the Literature using Artificial Intelligence

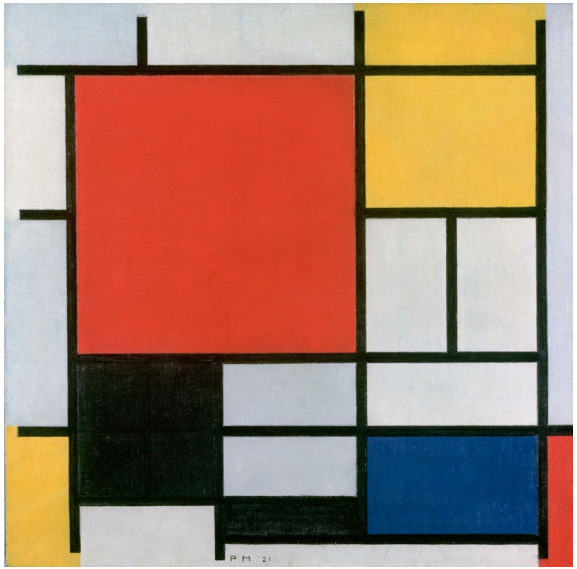
**Mark Kiel MD PhD**

*CSO and Co-Founder of Genomenon*

2025 NASEM Genomics Roundtable - Exploring Applications of AI in Genomics and Precision Health: A Workshop

# What is RWE?

# Clinical Trials vs. Real-World Evidence



Piet Modrian
*Composition in Red, Yellow, Blue and Black*
1921

**Clinical Trial Data**
is highly **controlled**, with **strict** protocols, pre-defined endpoints, and **carefully** selected patient populations, ensuring a high level of **purity** but limiting generalizability to broader populations

# Clinical Trials vs. Real-World Evidence

Jackson Pollock
*Number 1A, 1948*
1948

**Real-World Data**
is inherently more **diverse** and **messier** encompassing **unstructured** and semi-structured patient data from **disparate** real-world sources and settings like EHRs, claims data, and clinical literature

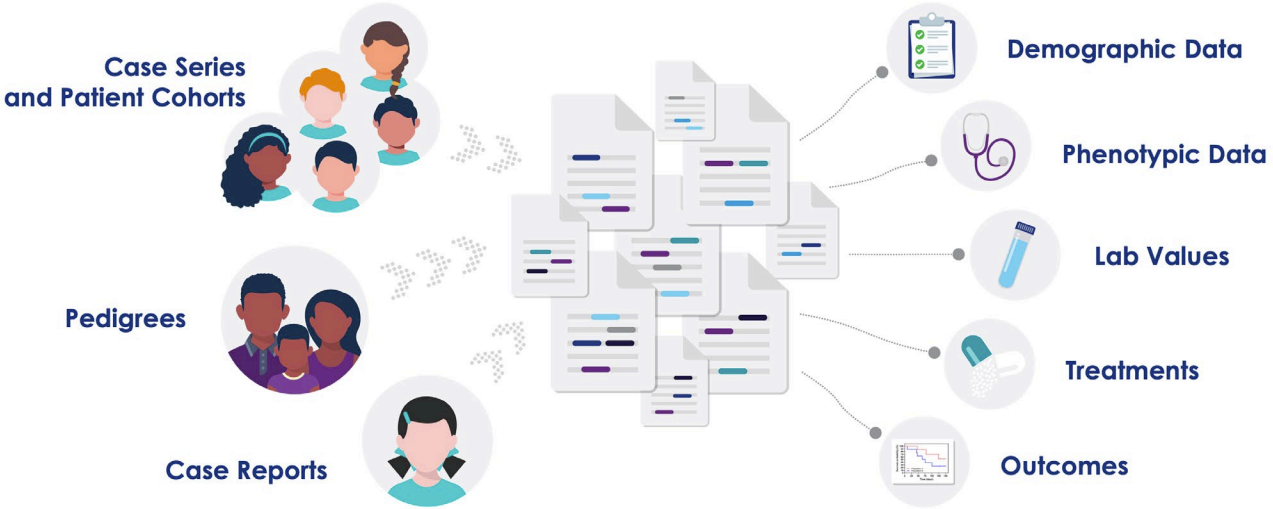
# Promise of and Challenges for RWD

**More Inclusive Discoveries**
**Improved Patient Outcomes**
**Accelerated Healthcare Innovation**

**Challenges include**

- data completeness
- data quality
- data complexity
- time to aggregate
- expense to access
- uncertainty of analysis

# Clinical Literature is a Valuable Source of RWD




# Clinical literature tells patients' stories through RWD

# Precision Medicine Applications of RWD

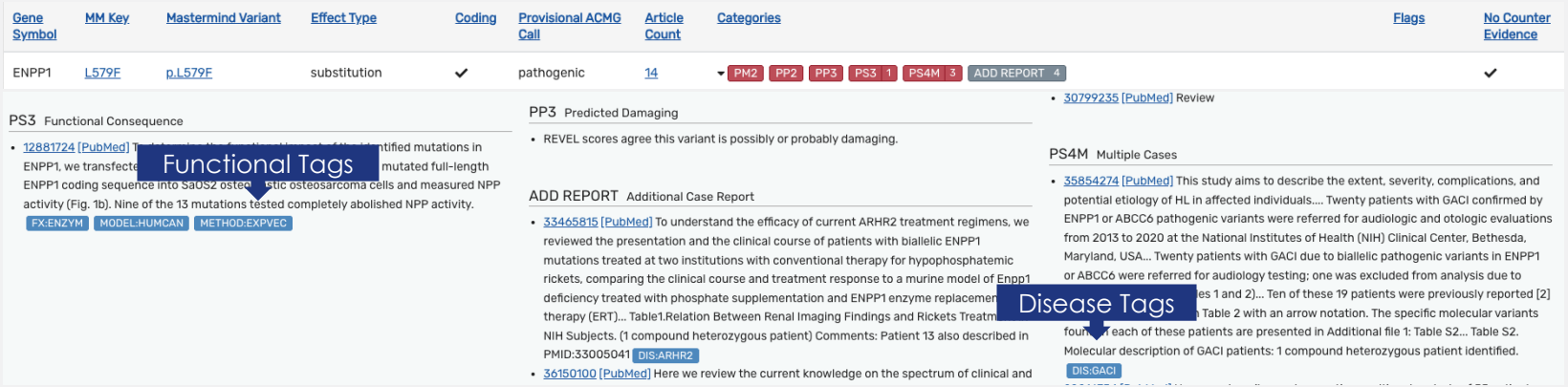
## Ideal sources for RWD for Rare Diseases and Precision Oncology

- **Data breadth** - patient types and patient numbers
- **Data depth** - data granularity per patient

# RWE Variant Landscapes

## Comprehensive ACMG-classified SNVs/indels with evidence citations, disease tags, and functional insights.

### *ENPP1* EXAMPLE






*Richards et al. 2015

# RWE Patient Landscapes

## Comprehensive patient database with demographic data, genotypes, and customizable clinical details for disease insights with citations.

### *ABCC6* EXAMPLE

+ Customizable lab tests, treatments, outcomes, etc.

| PMID | Patient ID | Age at Evaluation | Clinical Diagnosis | Phenotypes | Kidney Phenotype | Vascular Calcification | *ABCC6* Variant (cDNA) | *ABCC6* Variant (protein) | *ENPP1* variant(s) |
|---|---|---|---|---|---|---|---|---|---|
| 29713628 | 1 | 34 | None | Hypertension, Kidney stones | Yes | No | c.? | p.Arg1141Ter | No |
| 29713628 | 2 | 52 | None | Kidney stones | Yes | No | c.? | p.Arg807Gln | No |
| 31646622 | 3 | 11 | PXE | Retinal angioid streaks, cutaneous lesions, asthenia, peripheral artery disease, medial calcific sclerosis… | No | Yes | c.3421C>T | p.Arg1141Ter | Yes |

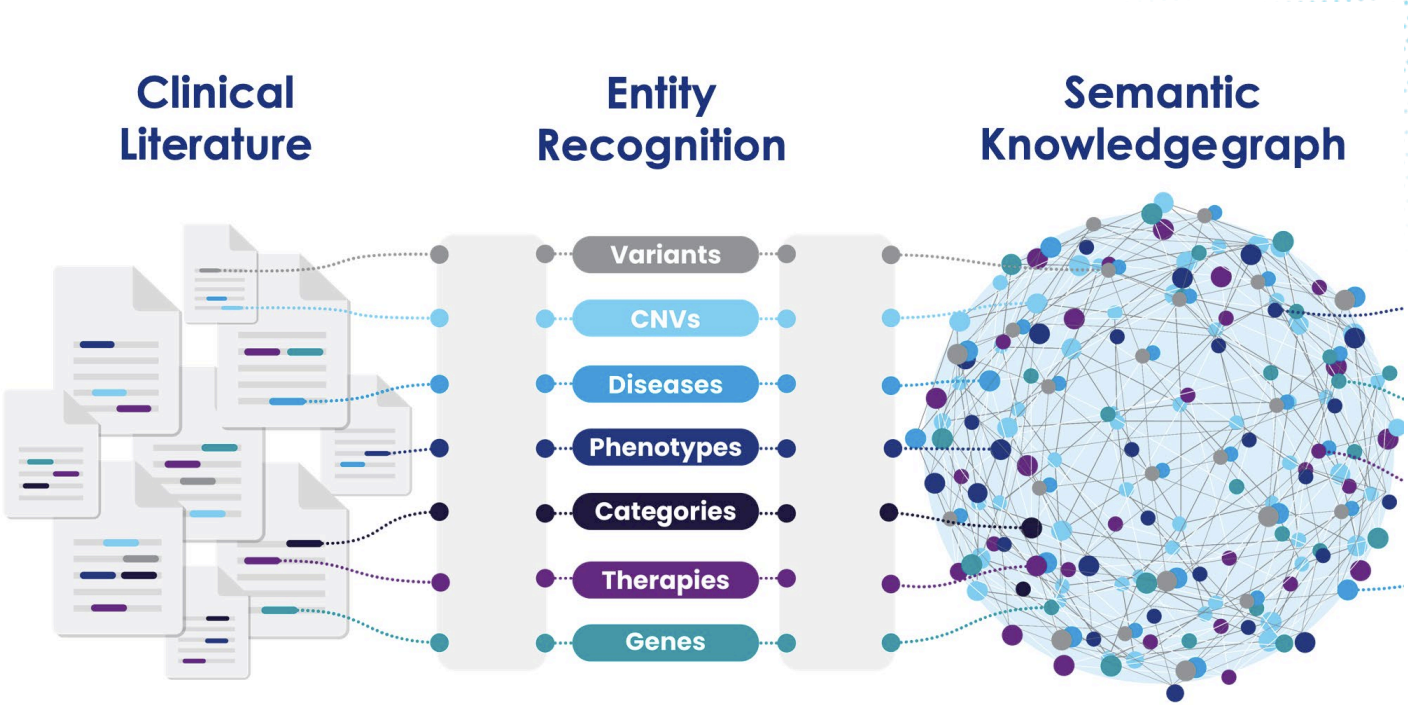
# How to Extract RWE from Published Literature?

WHO WE ARE:

# Genomenon provides *genomic intelligence* for clinical diagnostics and precision therapeutic development.

We simplify complex genetic data into actionable insights.

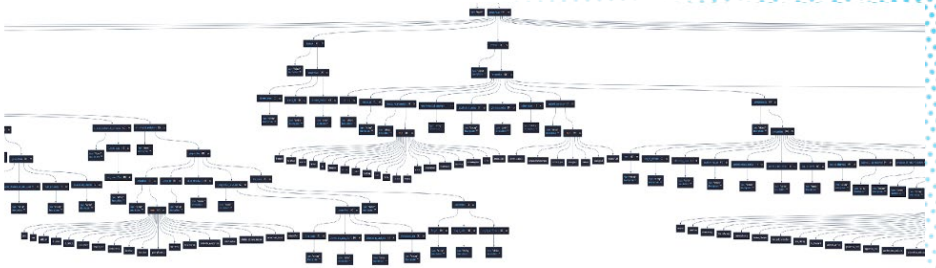
# What is G³ (Genomenon Genomic Graph)?



# How does G$^3$ work?

Extensive schema to index all clinical literature for a complete set of entities, properties, and relationships

Every entity, property, and relationship in this schema has a model prompt associated with it.



**15 Entities**

Gene
Protein
Variant
Disease
**Patient**
Phenotype/Symptom
Biomarker
Drug
Drug class
Molecular profile
Therapy
Treatment approach
Indication tumor type
Clinical trial

**~120 Entity Properties, with multiple nesting levels**

Id
Family id
Family relationship
Genotype (HGVS)
Genotype notes
Biochemical notes
Other notes
Zygosity
Demographics
**Outcome**

**Response**
Remission
Relapse
Adverse effects
Progression
Tolerability
Stabilization
Survival rate
Quality of life
Non responder
Treatment adherence
Biomarker response
Cure
Symptomatic relief

**Positive**
Negative
Partial
Complete

**~30 Entity to Entity Relationship Types**

{Subject} **{Relationship Predicate}** {Object}

Clinical trial **tests** drug

Disease **occurs in** patient

Biomarker **is marker for** disease

Drug **treats** patient

# What can G$^3$ do?

**Entities**
Identify terms in papers and map to ontologies

**Properties**
Identify traits and characteristics linked to matched entities

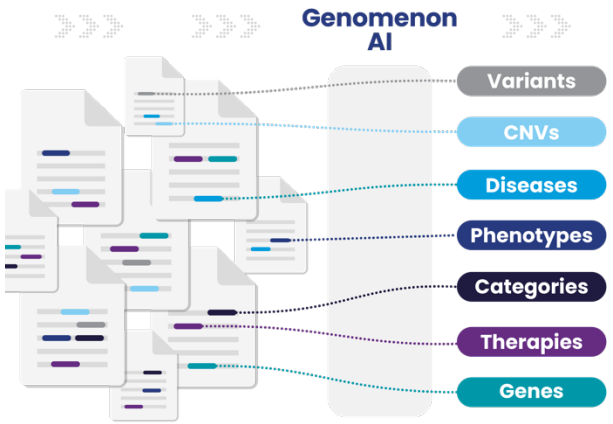
**Relationships**
Understand how terms are inter-related in articles

**Databases**
Output custom databases to custom specifications

**Summaries**
Produce natural language text summaries and answer questions

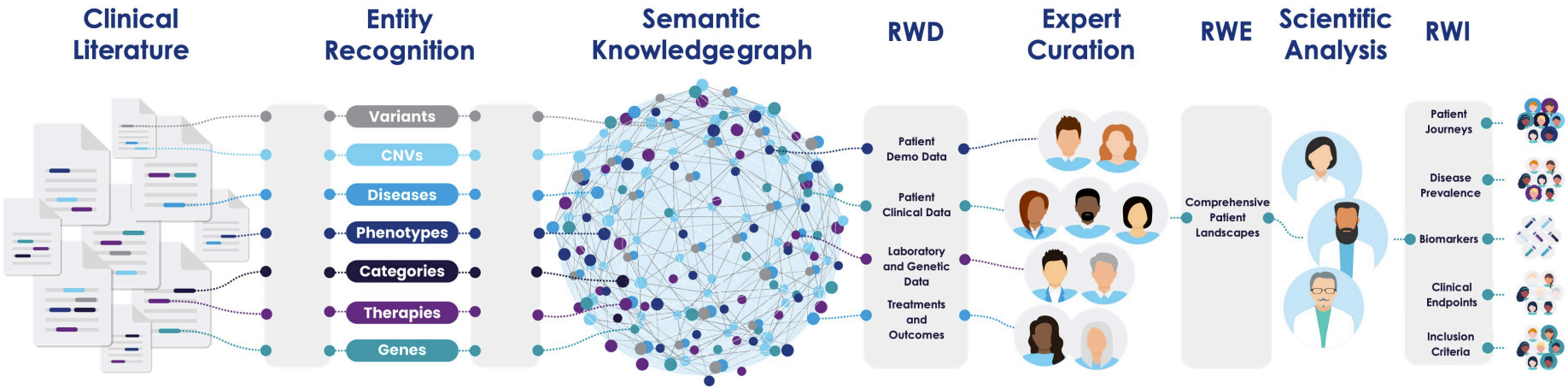
# Combining Expert Curation with Artificial Intelligence

**Sophisticated Computation**




**Dedicated Genetic Experts**

# How does it all fit together?




## Combinatorially! Corpus, Computation, Curation

# Indexed and Curated Databases of Genomic Variants


**The standard in evidence-based interpretation of complex cancer profiles**

Query and access curated information on variants, FDA drug labels, targeted therapies, pre-clinical and clinical evidence and clinical trials in over 2200 genes


**Using AI and Genomic expertise to accelerate patient diagnosis**

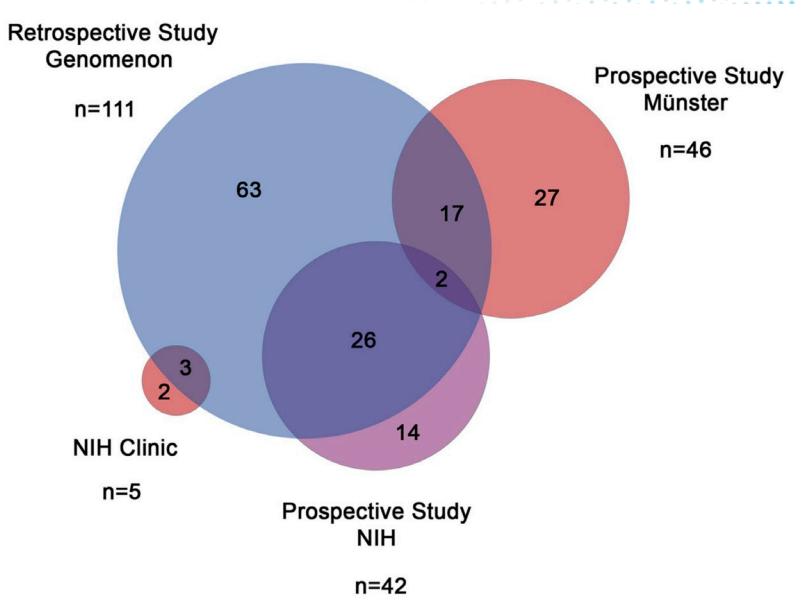
Across ~11M full-text genomic articles, 3.7M+ supplemental datasets, and 27M+ variants including curated genomic data for pathogenicity classification with supporting evidence

# What are Some Real-World Applications of RWE?

# *Inclusion Criteria and Disease Prevalence to Inform Trial Design and Market Strategy*

inozyme pharma

**Reanalyzed 1,500 *ENPP1* variants and patient cases, helping to design a successful PhII trial and re-calculate GACI prevalence from 1/200,000 to 1/64,000 to help identify and diagnose more patients.**



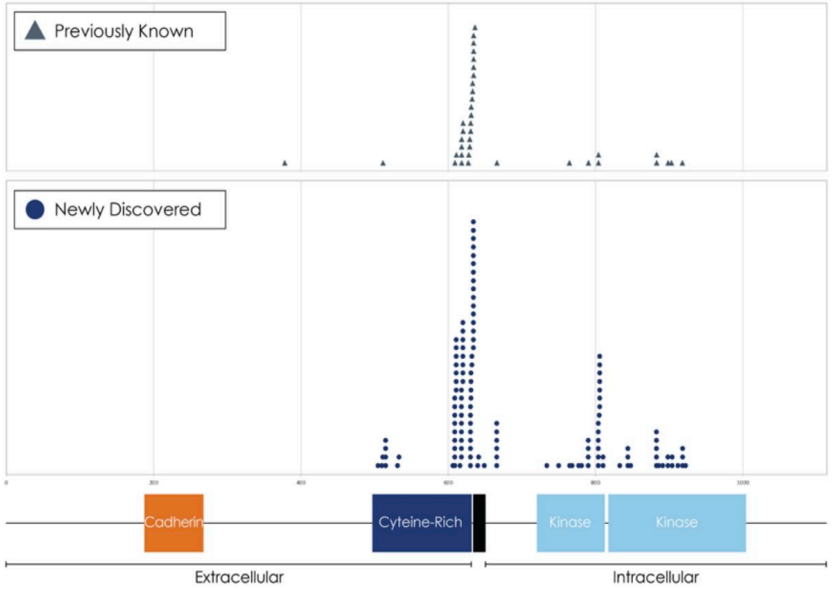



Chunn et al. 2022 [36461014]
Estimation of ENPP1 deficiency genetic prevalence using a comprehensive literature review and population databases

# *Expanded Inclusion Criteria for Regulatory Submission*

LOXO ONCOLOGY at Lilly

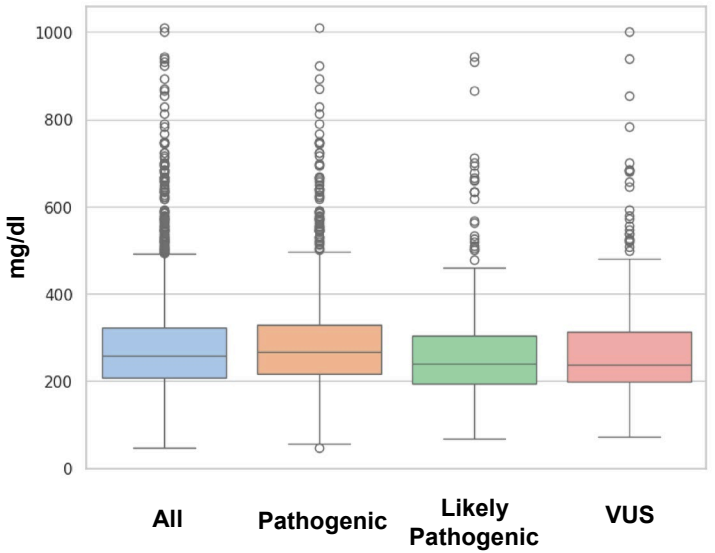
**Reclassified 3,800 *RET* variants, expanding Selpercatinib trial inclusion from 33 to 138, enabling broader patient enrollment.**



# *Clinical Biomarkers to Influence Clinical Practice*

ultragenyx

**Analyzed 42,000 FH patients, showing *LDLR* VUS mirror pathogenic variants, demonstrating literature-based RWE can refine FH diagnosis to diagnose more patients.**



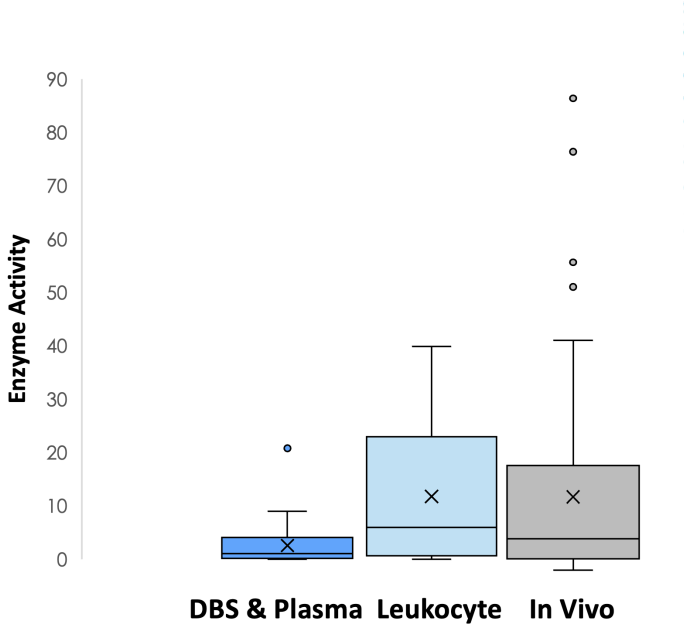



Mathias et al. 2024
Variant classification is impacted by the presence of biochemical data in published patient reports: A case study for Familial Hypercholesterolemia

# *Functional Biomarkers for Regulatory Submission*

Amicus Therapeutics®

**Analyzed ~1,500 *GLA* variants, supporting higher enzyme thresholds (3–5.5%), expanding Fabry diagnosis and influencing regulatory approval to treat more patients.**






Bissonnette et al. 2025
Systematic Literature Review of GLA Variants Uncovers Additional Fabry Disease-Causing Variants

# *Patient Stratification to Identify Therapy-Responsive Populations*

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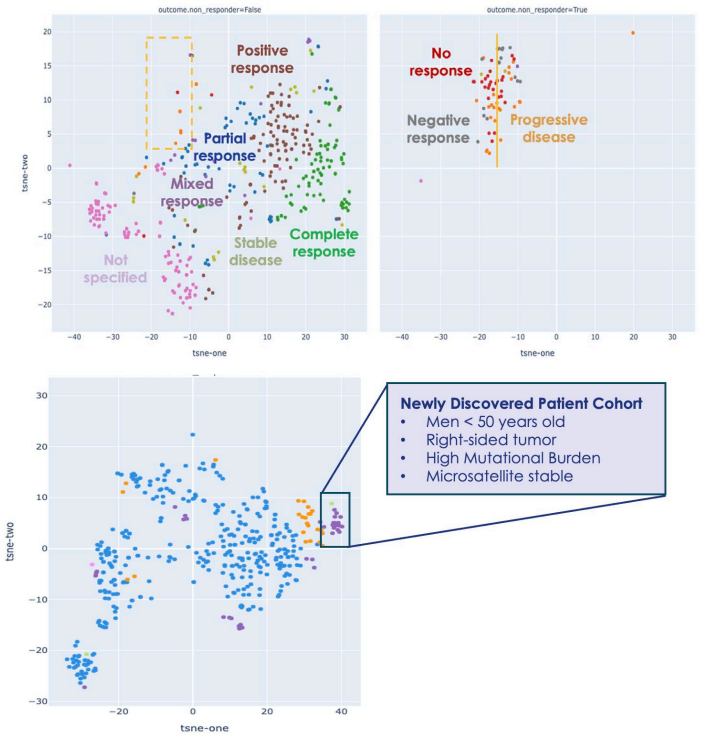
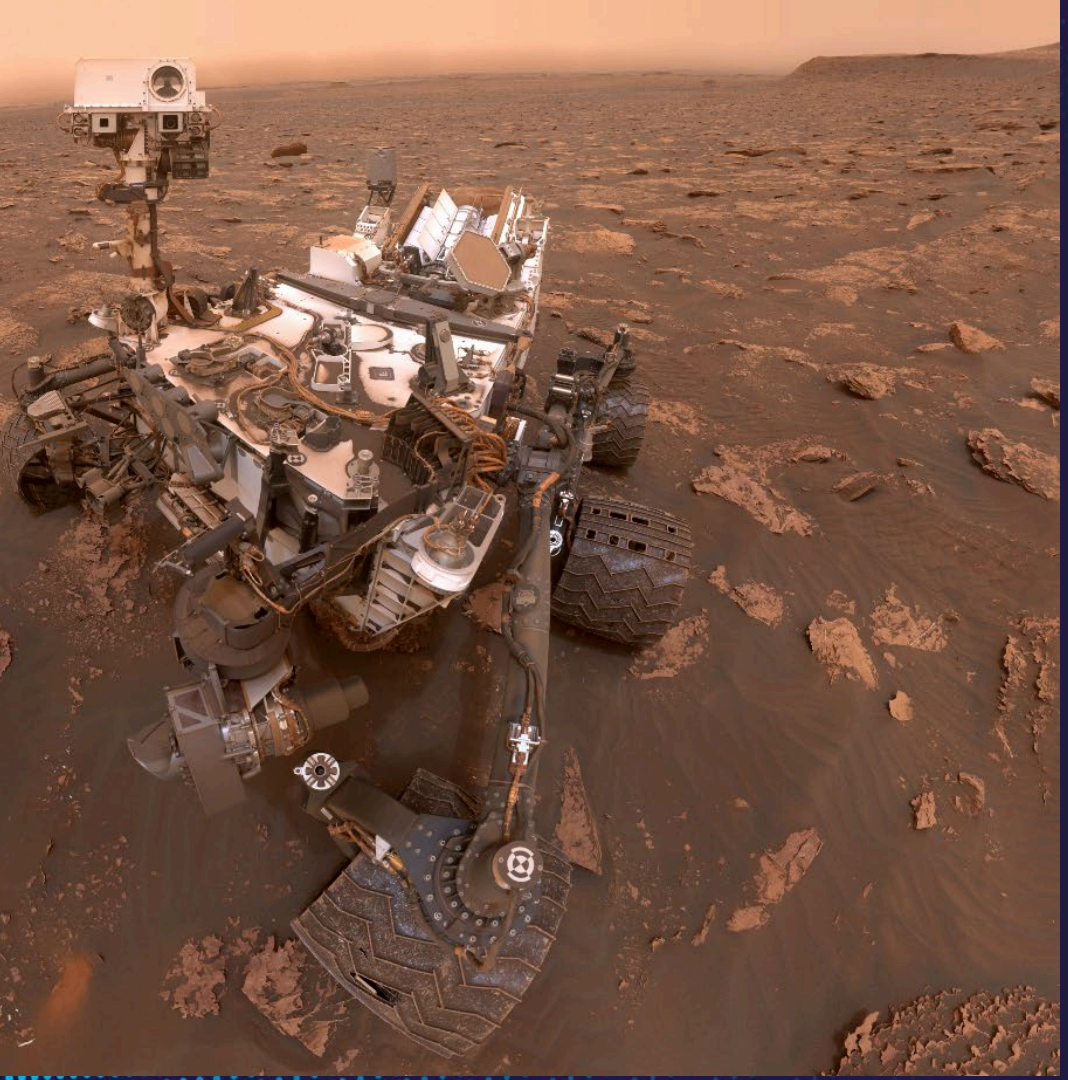
**Identified a 5% subpopulation of CRC patients with favorable immunotherapy response, enabling patient stratification**






Eads et al.
manuscript in preparation

# Newborn Screening by Sequencing



# Automation and Optimization of Clinical and Commercial Drug Development

# Drug Development Activities with Potential for Semi-Automation

| Discovery | Pre-Clinical | Clinical Development | Regulatory | Commercialization |
|---|---|---|---|---|
| **Disease Understanding** | **Model Validation** | **Trial Design** | **Initial Approvals** | **KOL Engagement** |
| **Target Identification** | **Target Validation** | Trial Feasibility | **Label Expansions** | **Publications & Congress** |
| **Biomarker Discovery** | **Biomarker Identification** | Trial Execution | Post-Marketing Surveillance | **Market Segmentation** |
| **Patient Stratification** | **Safety Signal Exploration** | **Regulatory Submissions** | HTA and Reimbursement | Brand Differentiation |
| **Preclinical Validation** | **Translational Relevance** | Payer/HTA Engagement | Bridging Data | Launch Readiness |
| **Trial Design Planning** | **Portfolio Strategy** | | Regulatory Science | Post-Launch Monitoring |
| Protocol Feasibility | **Orphan Indication Targeting** | | HTA Submissions | **Scientific Communication** |
| **Indication Expansion** | | | Reimbursement Support | |
| **Portfolio Prioritization** | | | Pricing Strategy | |
| Competitive Landscape | | | Economic Models | |
| | | | Global Market Access | |
| | | | Post-Launch Performance | |

# THANK YOU

**Mark Kiel**
CSO, Co-Founder
kiel@genomenon.com

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