



## CLARITY<sub>PV</sub>: from Safety Pharmacology to Postmarketing surveillance

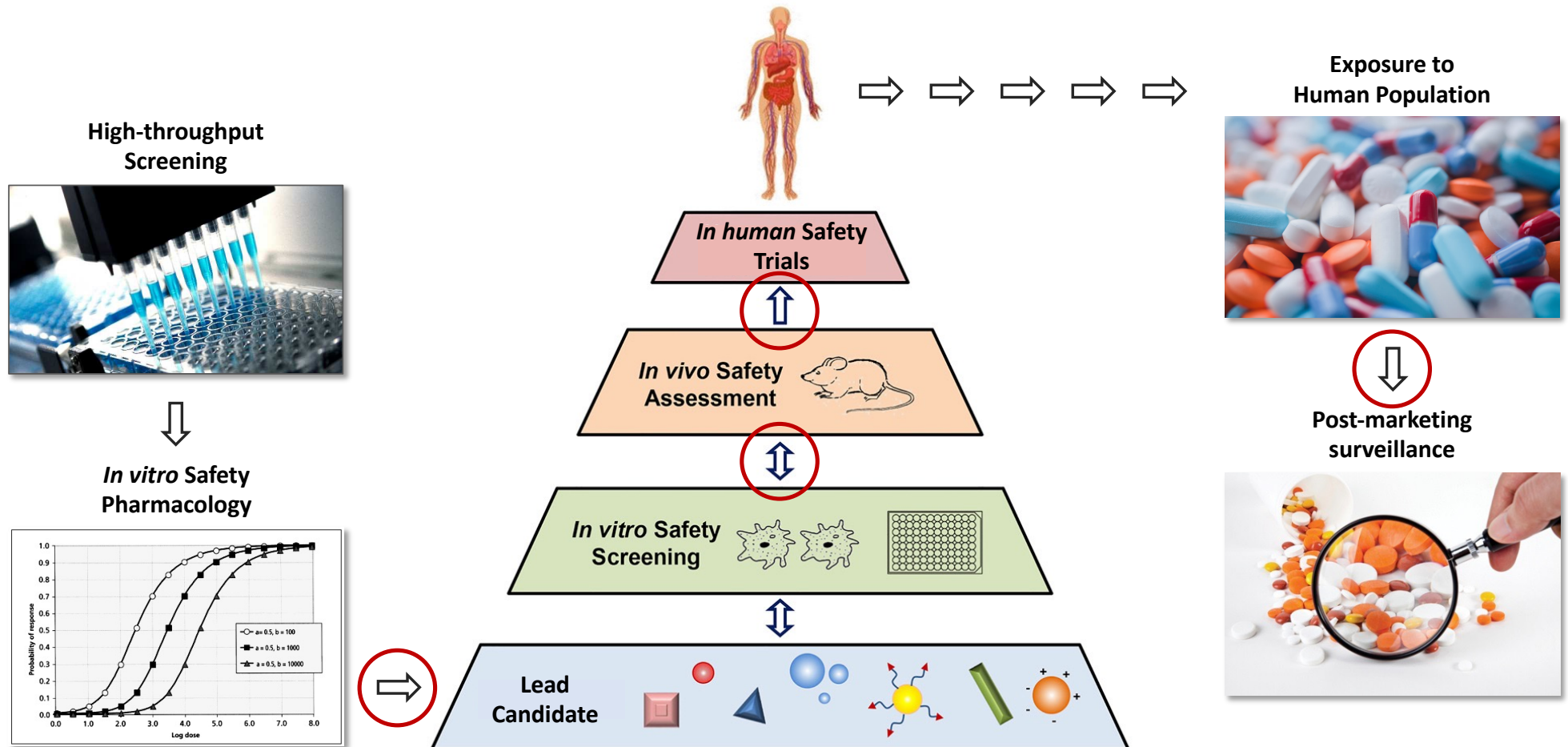
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**Dr. Jordi Mestres**

Founder & CSO, Chemotargets



# Translational Safety: the issues



Adapted from Mirshafiee et al. *Molecular Therapy* 2017

# Translational Safety: the solutions

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## **DATA**

Integrated safety data across the lifetime of the drug

- Safety pharmacology
- Preclinical toxicology
- Clinical safety
- Postmarketing surveillance

# Translational Safety: the solutions

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## **REPORTING**

Facilitate collecting periodic safety update reports

- Immediate access to postmarketing data updates
- Postmarketing surveillance of clinical safety events
- Stratified identification of postmarketing signals
- Reporting velocity and evolution of adverse events and reactions



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## FORECAST

Anticipate postmarketing adverse reaction signals

- Identification of prior markers
- Detection of translational safety issues
- Early projection of safety trends for new drugs on the market
- Define surveillance watch lists of drugs and side effects

# Translational Safety: the solutions

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Anticipate postmarketing adverse reaction signals

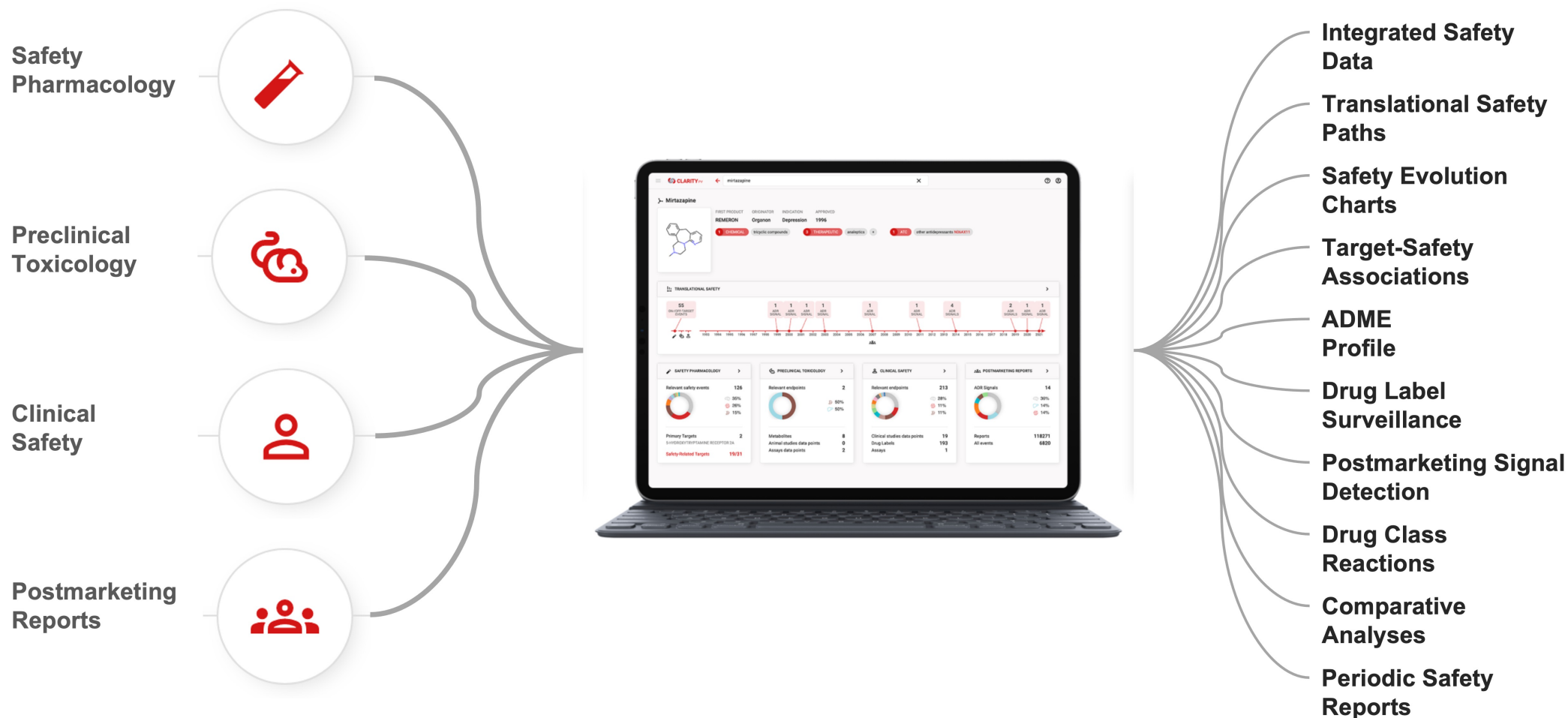
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## ANALYTICS

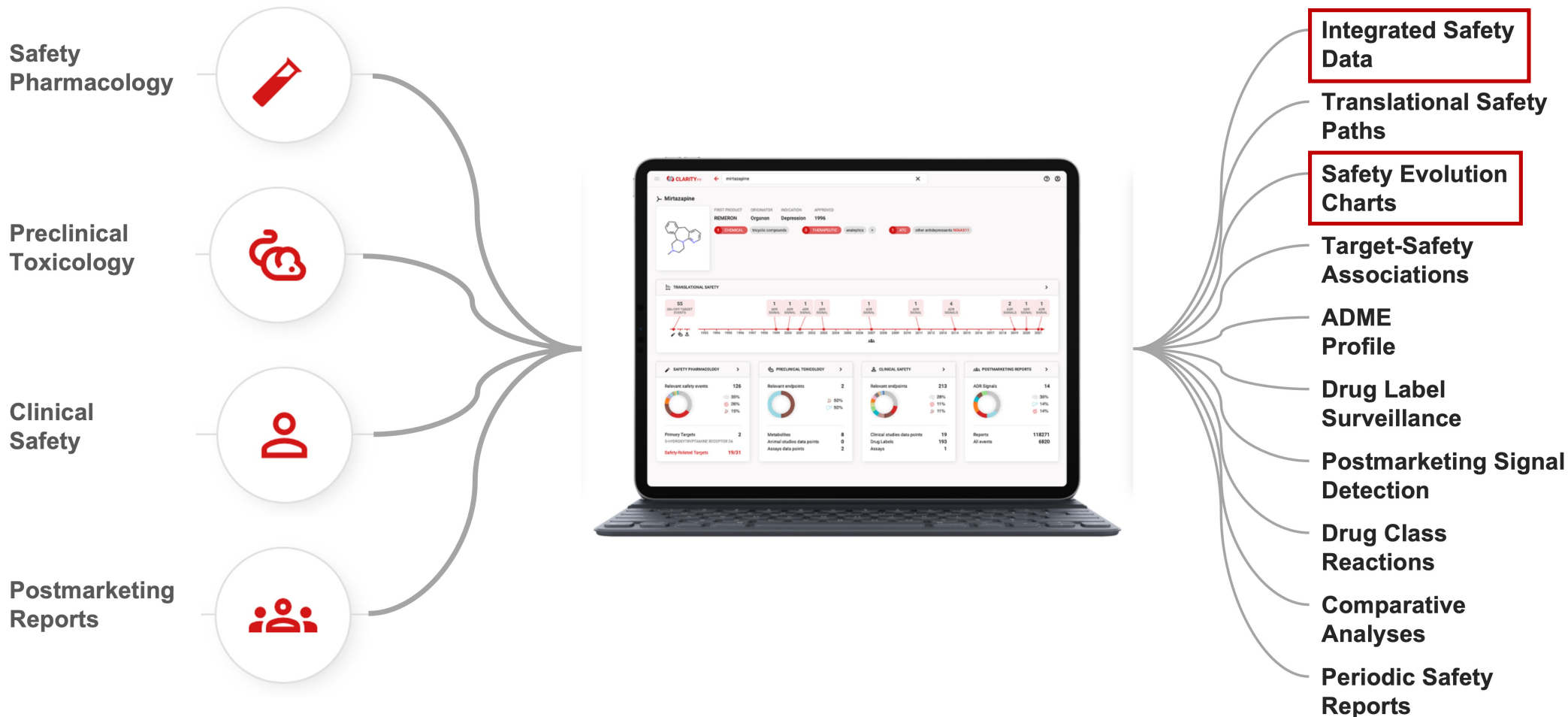
Interactive visualization tools

- Stratified analyses
- Translational safety
- Comparative analyses
- Safety forecast

# CLARITY<sup>PV</sup>: integrated data, reporting, forecast and analytics platform

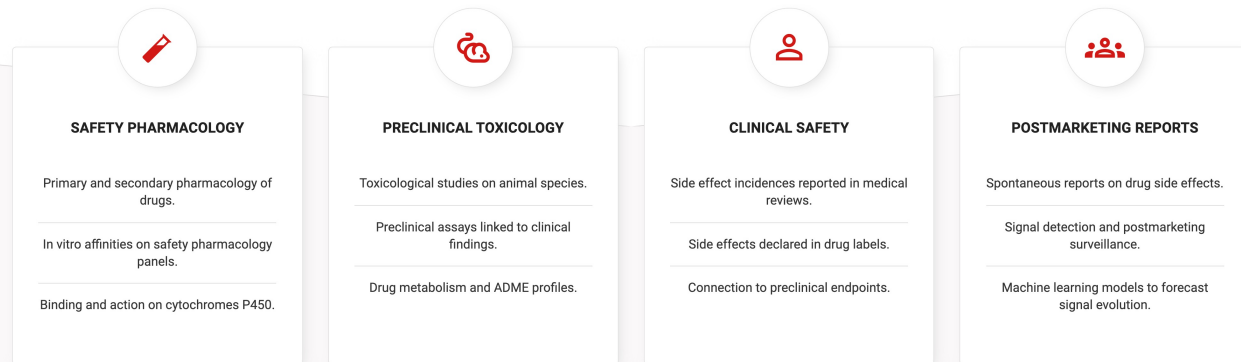


# CLARITY<sup>PV</sup>: integrated data, reporting, forecast and analytics platform

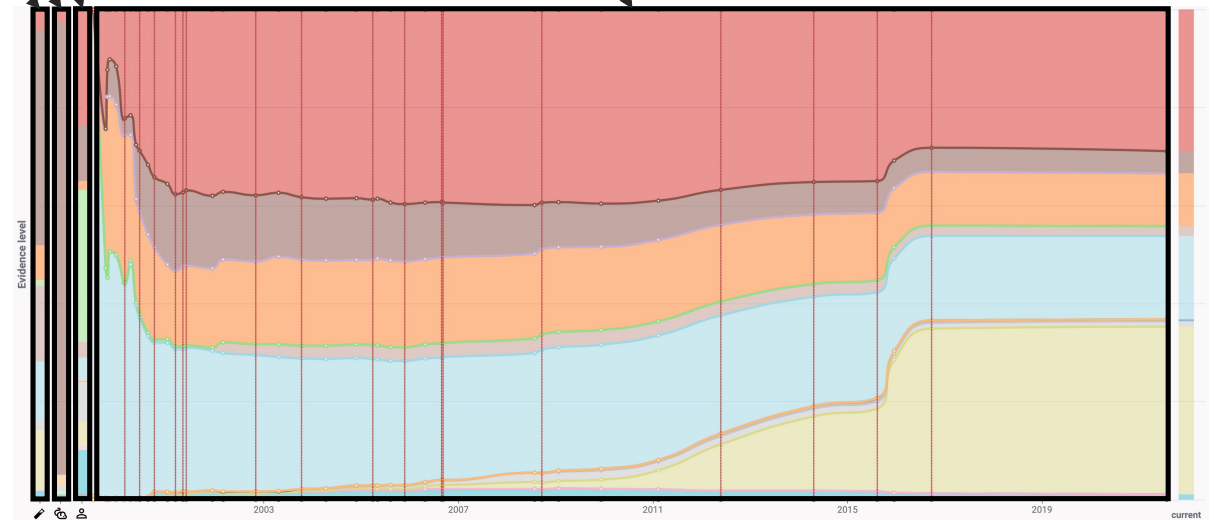


# Use Case: translational safety charts

From integrated safety data...



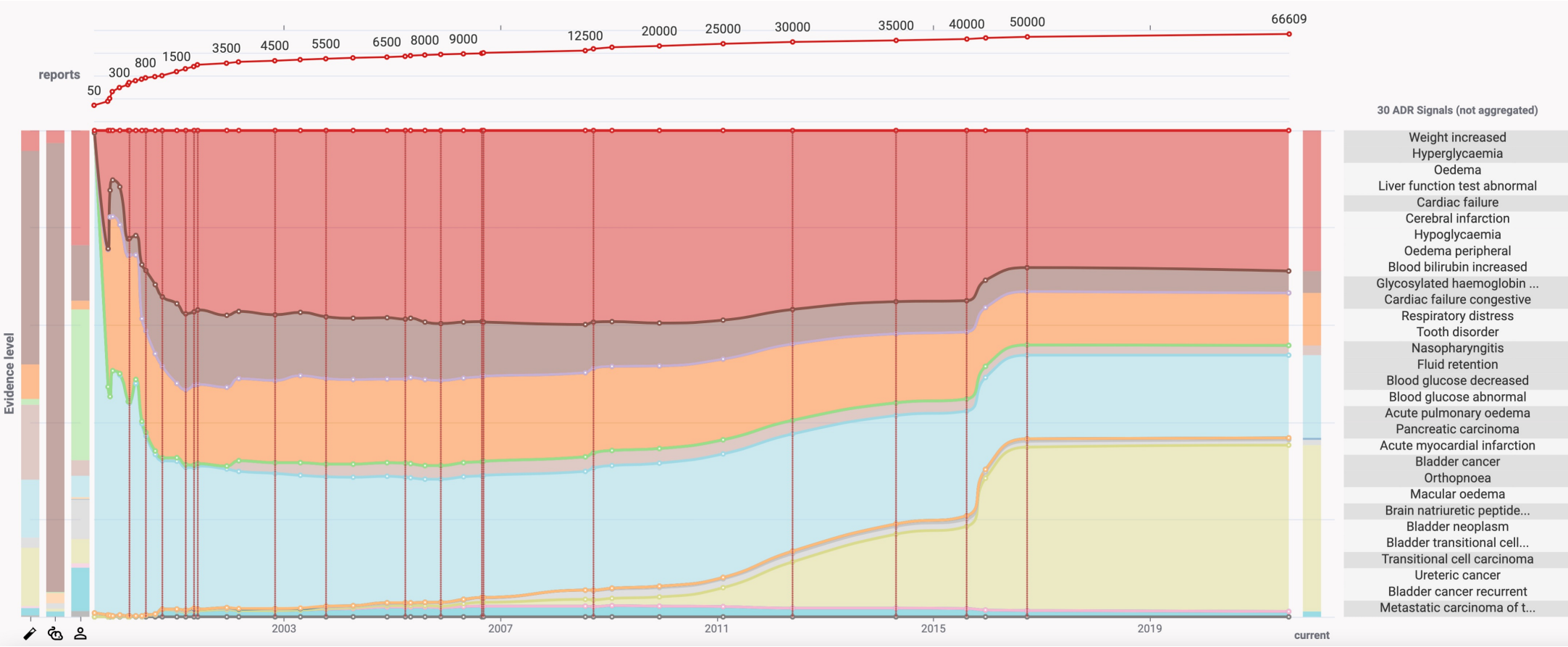
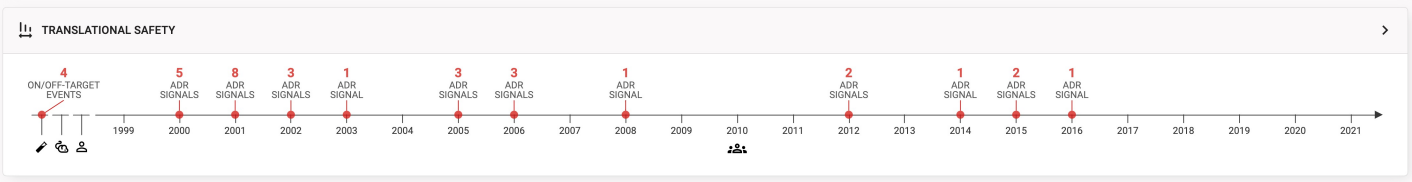
...to translational safety charts





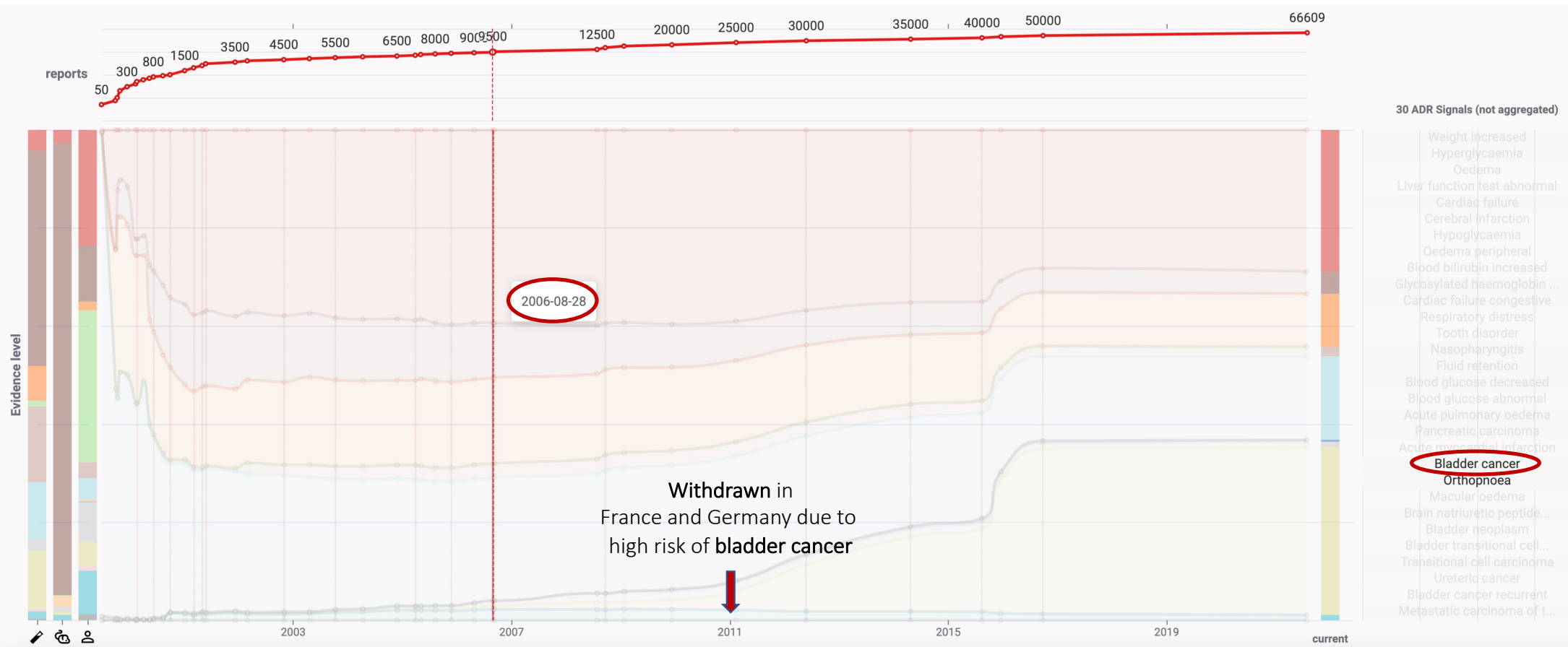
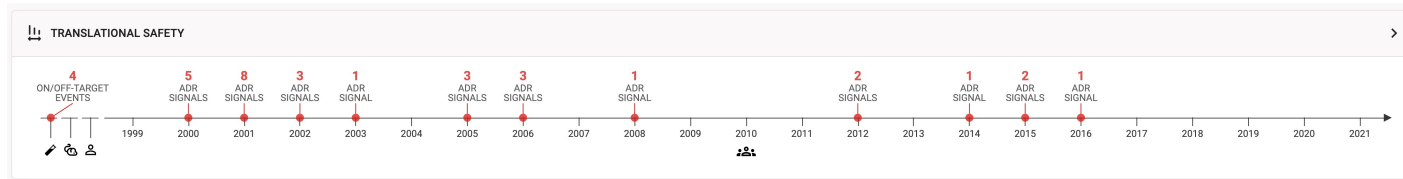
# Use Case: translational safety charts

Example: pioglitazone



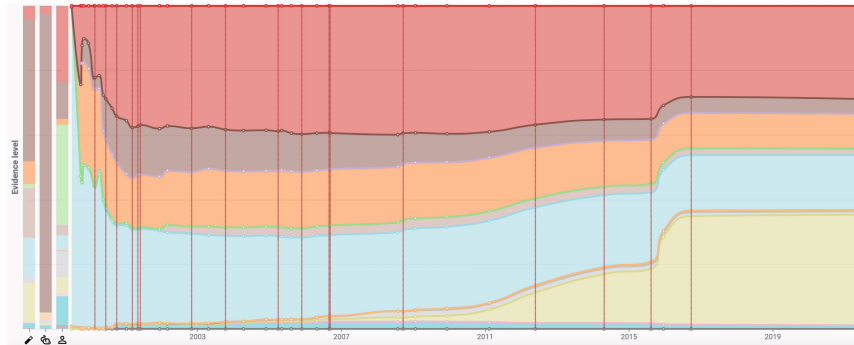
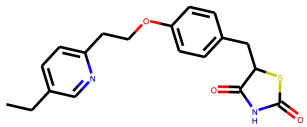
# Use Case: translational safety charts

Example: pioglitazone



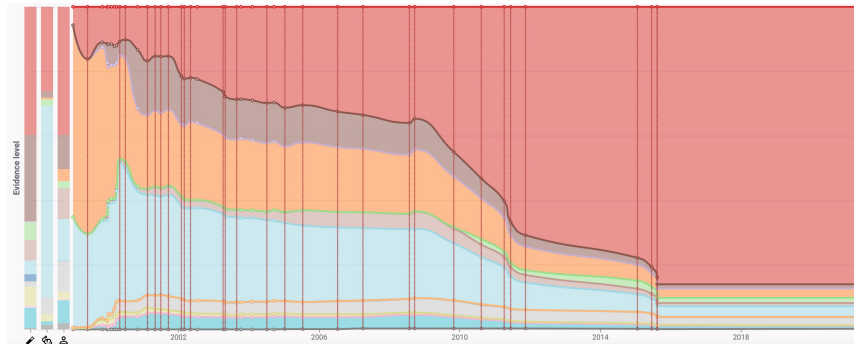
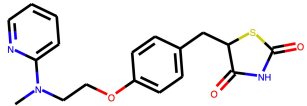
# Use Case: translational safety charts – comparative analysis

 Pioglitazone



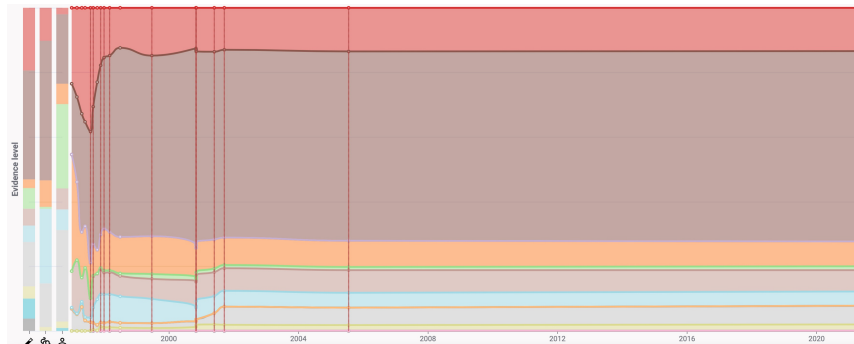
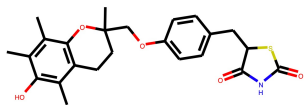
Renal and Urinary System

 Rosiglitazone



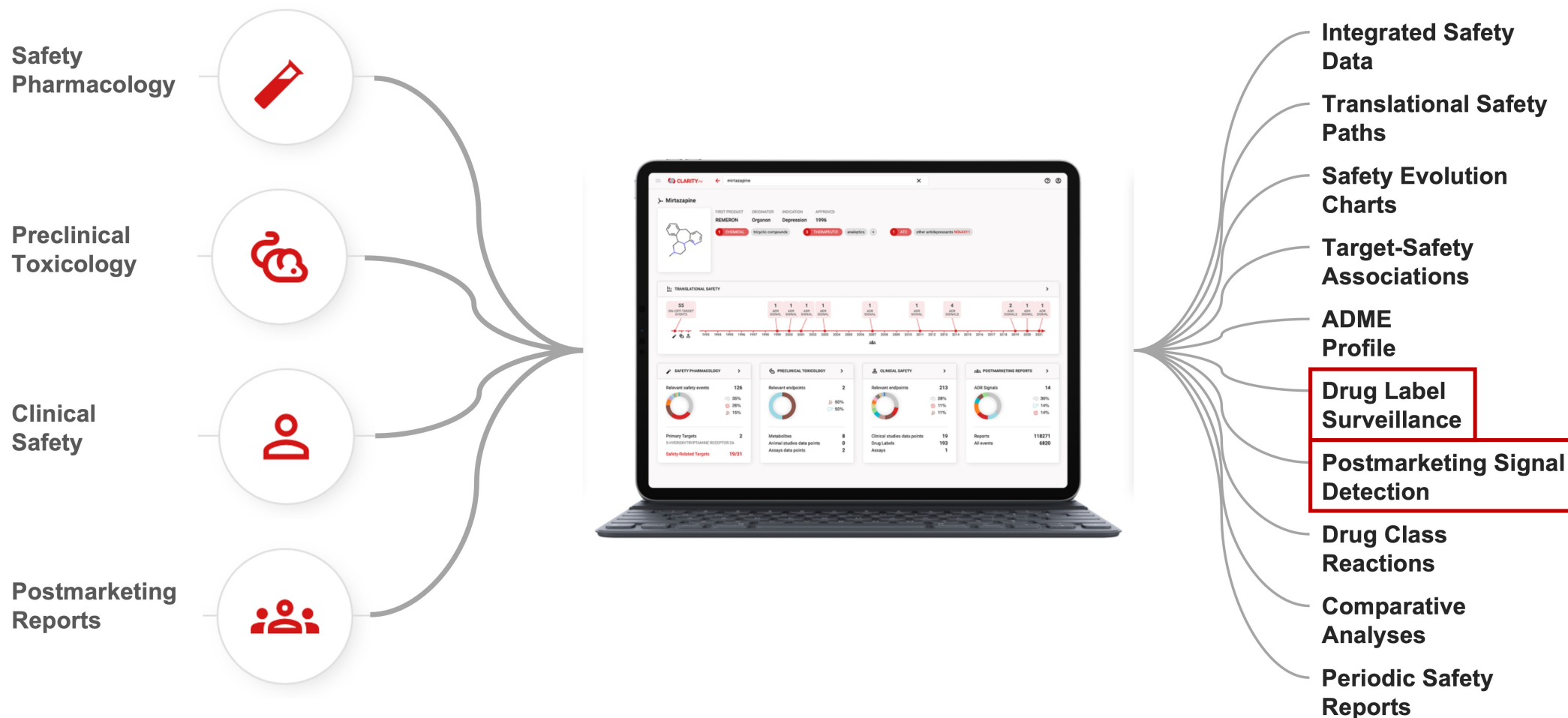
Circulatory System

 Troglitazone



Digestive and Excretory System

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# Use Case: postmarketing signal detection

From safety events in the drug label...



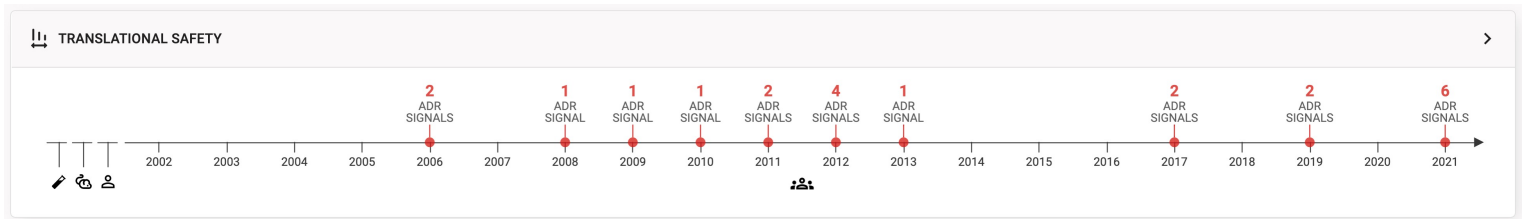
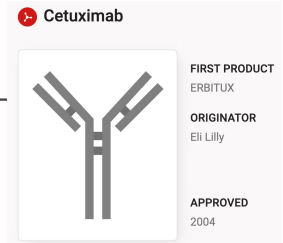
**LABEL: ERBITUX- cetuximab solution**

**DRUG LABEL INFORMATION**

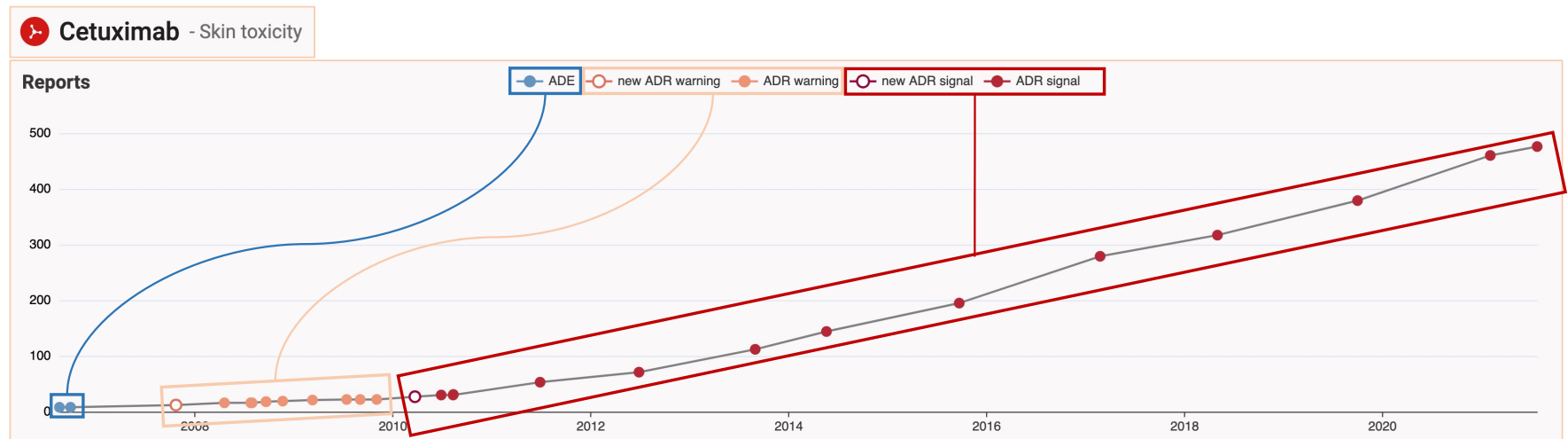
**5 WARNINGS AND PRECAUTIONS**

## 5.4 Dermatologic Toxicity

ERBITUX can cause dermatologic toxicities, including acneiform rash, skin drying and fissuring, paronychia inflammation, infectious sequelae (for example, *S. aureus* sepsis, abscess formation, cellulitis, blepharitis, conjunctivitis, keratitis/ulcerative keratitis with decreased visual acuity, cheilitis), and hypertrichosis.



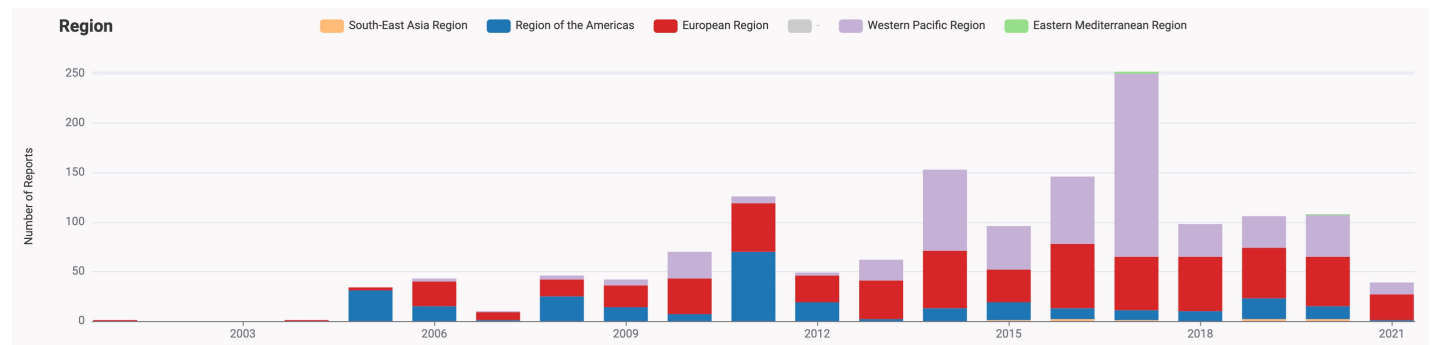
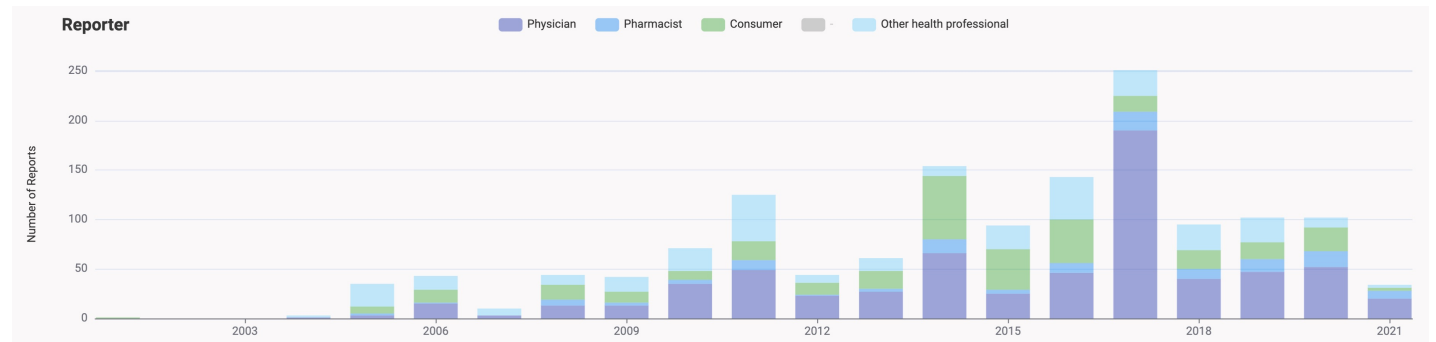
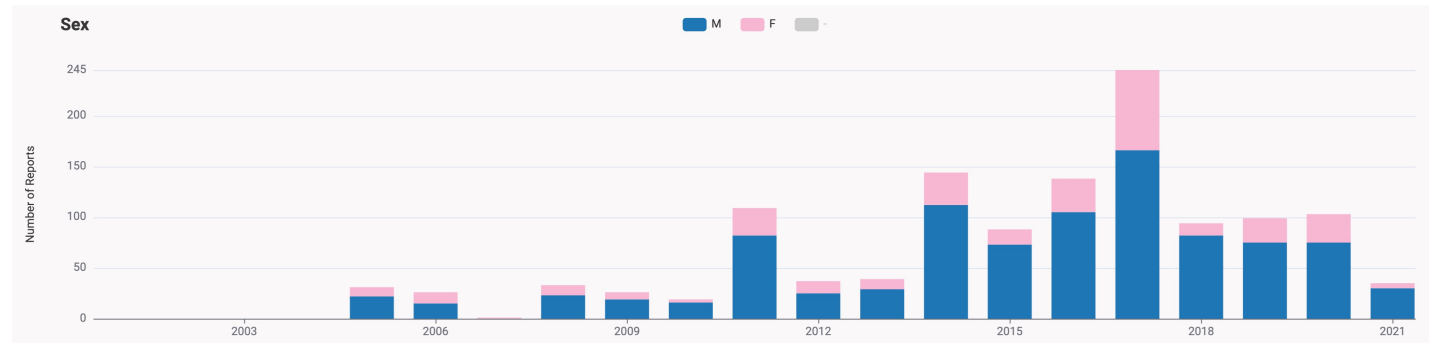
...to reaction signals in postmarketing reports





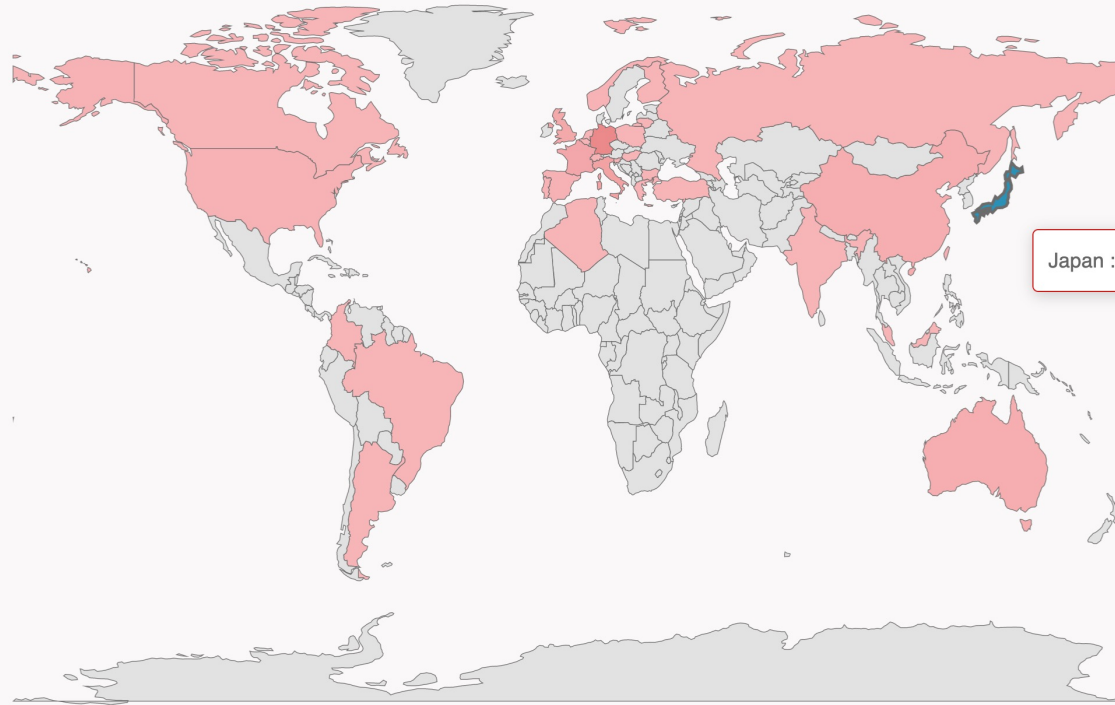
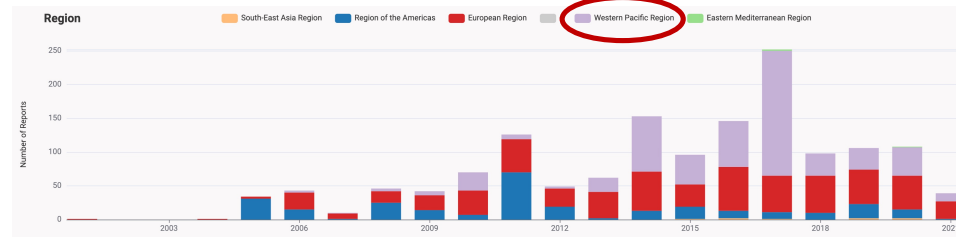
# Use Case: postmarketing report analysis

## Cetuximab - Dermatitis acneiform

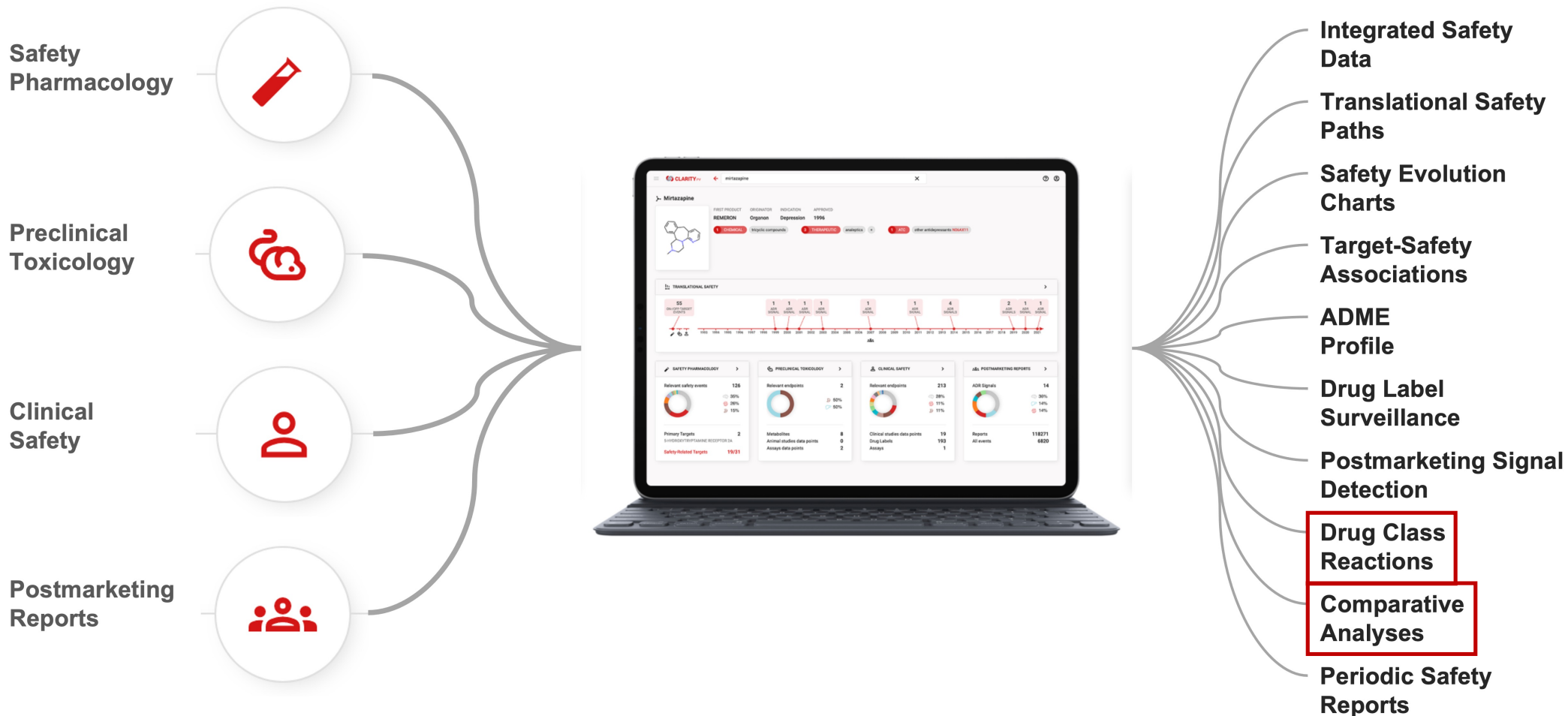


# Use Case: postmarketing report analysis

 **Cetuximab** - Dermatitis acneiform



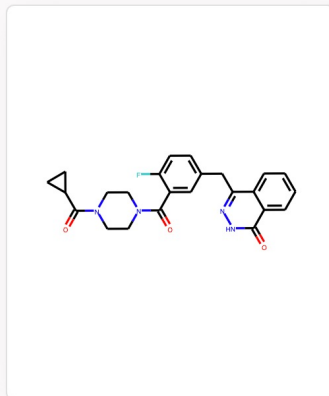
# CLARITY<sup>PV</sup>: integrated data, reporting, forecast and analytics platform



# Use Case: comparative analyses

Example: PARP inhibitors

## Olaparib

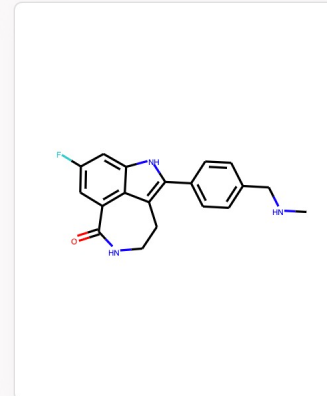


**FIRST PRODUCT**  
LYNPARZA

**ORIGINATOR**  
AstraZeneca

**APPROVED**  
2014

## Rucaparib

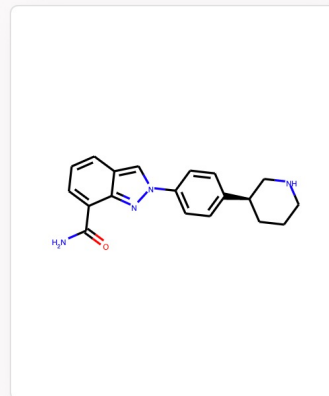


**FIRST PRODUCT**  
RUBRACA

**ORIGINATOR**  
Clovis Oncology

**APPROVED**  
2016

## Niraparib

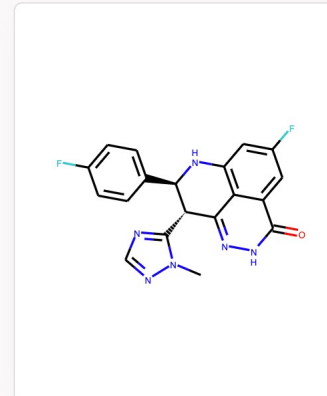


**FIRST PRODUCT**  
ZEJULA

**ORIGINATOR**  
Tesaro

**APPROVED**  
2017

## Talazoparib



**FIRST PRODUCT**  
TALZENNA

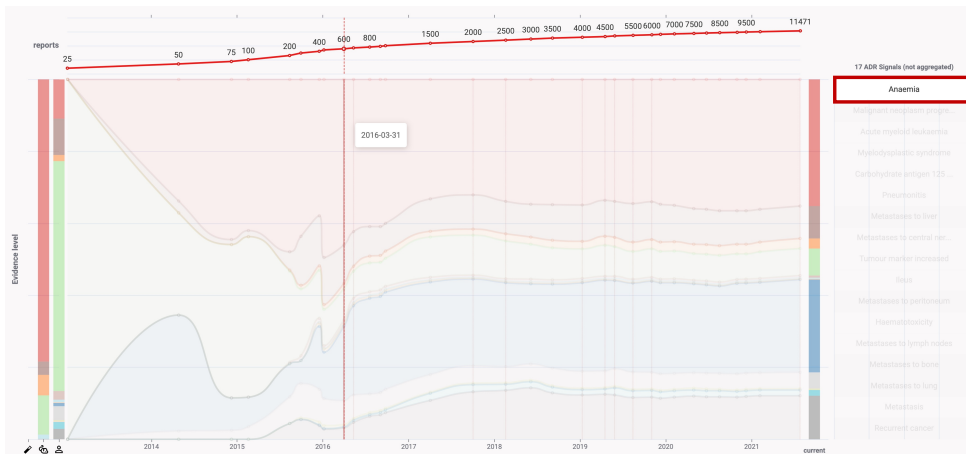
**ORIGINATOR**  
Pfizer

**APPROVED**  
2018

# Use Case: comparative analyses – class reaction: anaemia

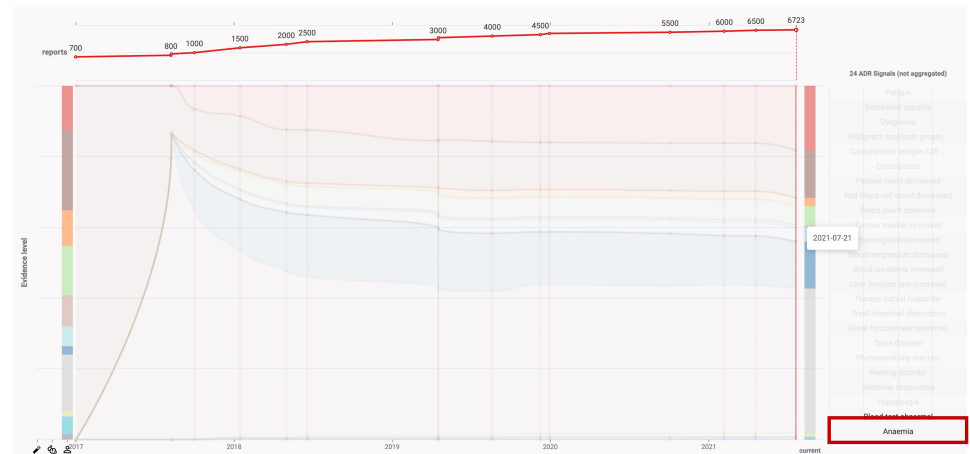
## Olaparib

approved: 2014



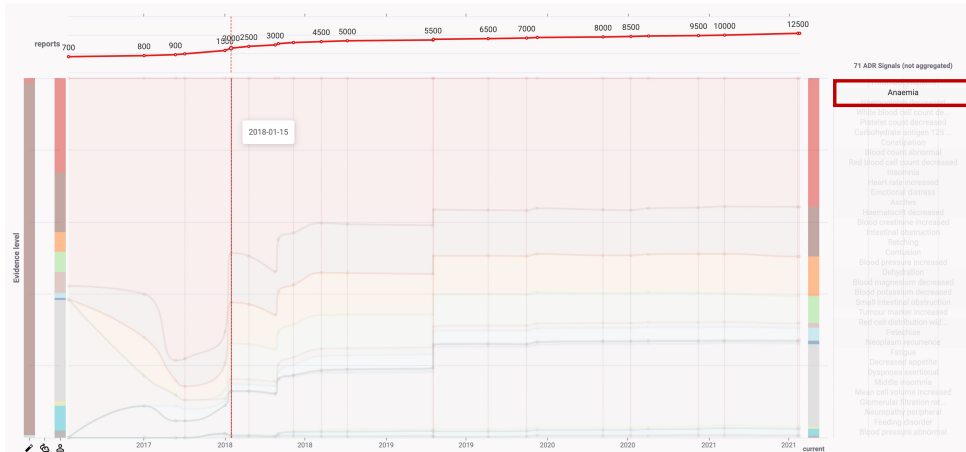
## Rucaparib

approved: 2016



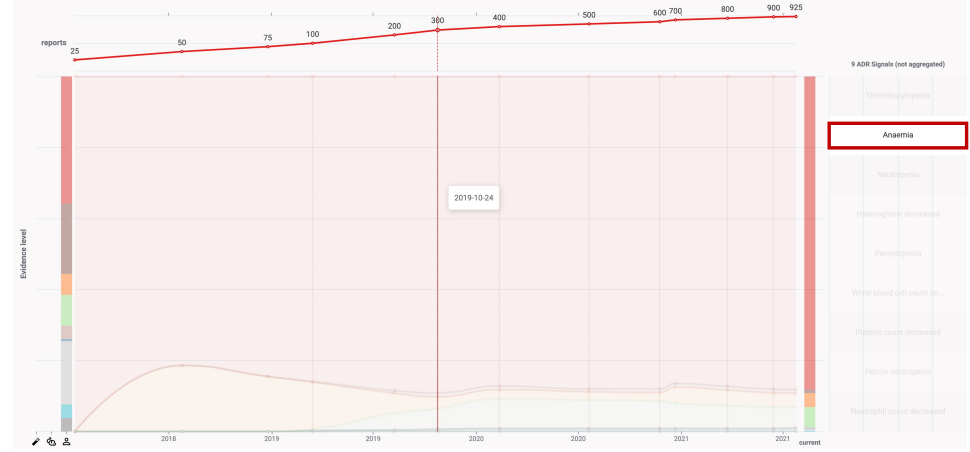
## Niraparib

approved: 2017



## Talazoparib

approved: 2018



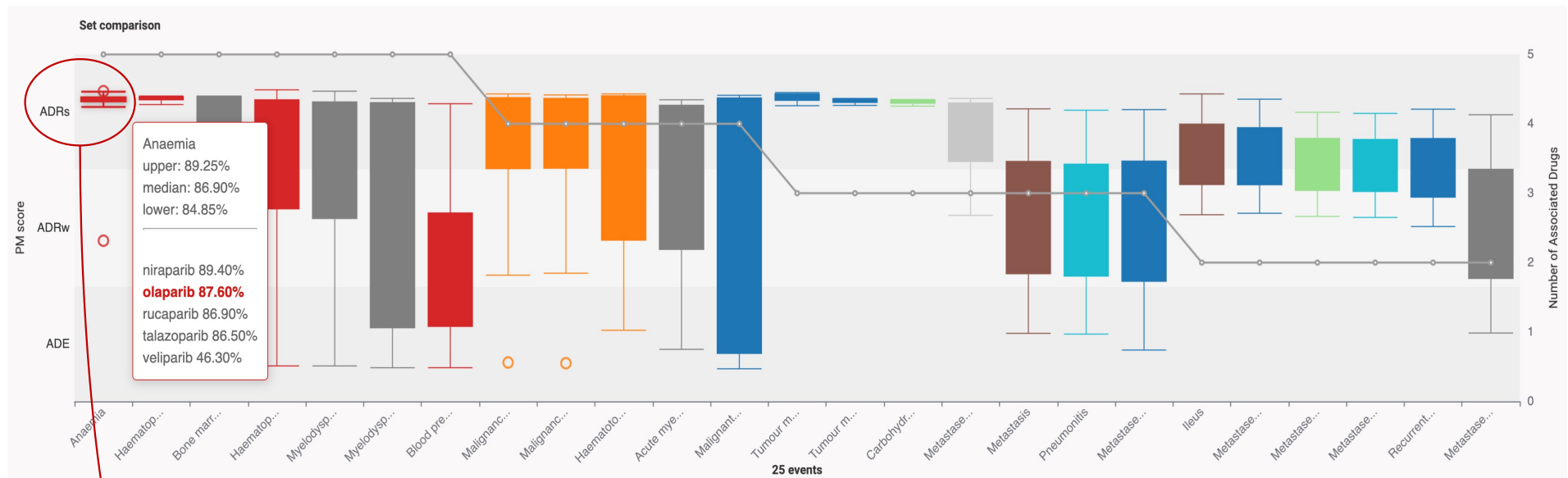


# Use Case: comparative analyses – class reaction: anaemia

Example: PARP inhibitors

5 [L01XK] POLY (ADP-RIBOSE) POLYMERASE (PARP) INHIBITORS ✕

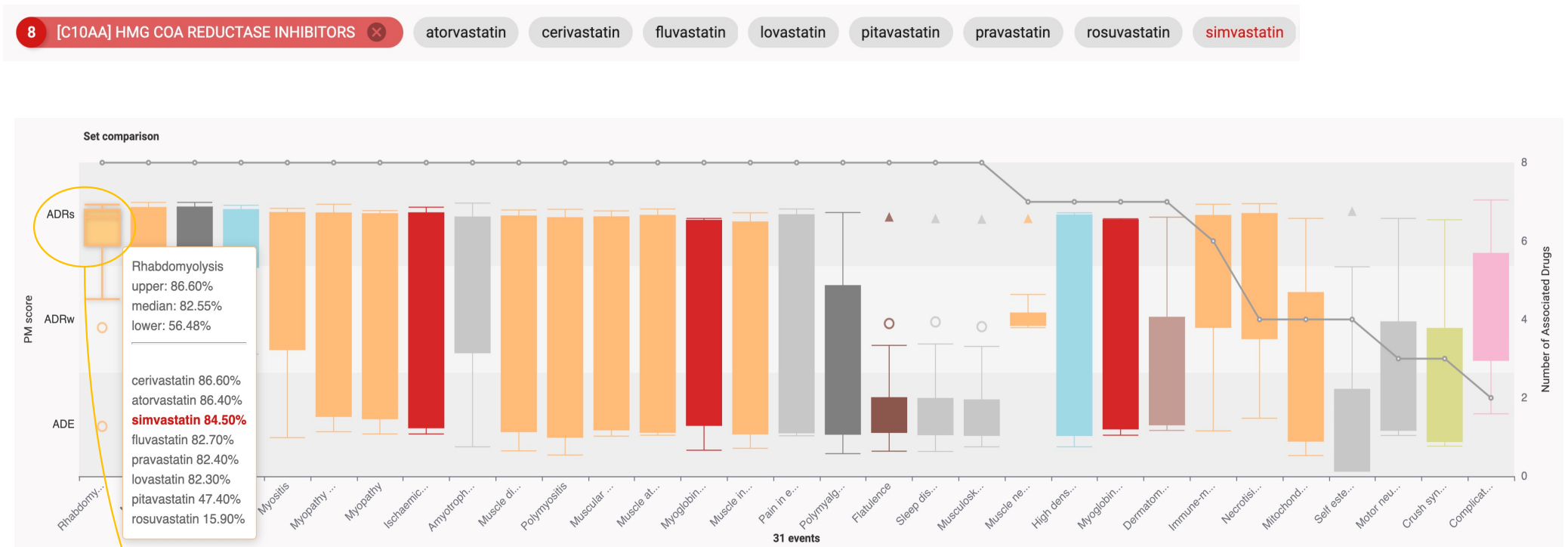
niraparib olaparib rucaparib talazoparib veliparib



**Anaemia** is an Adverse Drug Reaction signal (ADRs) for the entire class of PARP drugs currently in the market

# Use Case: comparative analyses – class reaction: rhabdomyolysis

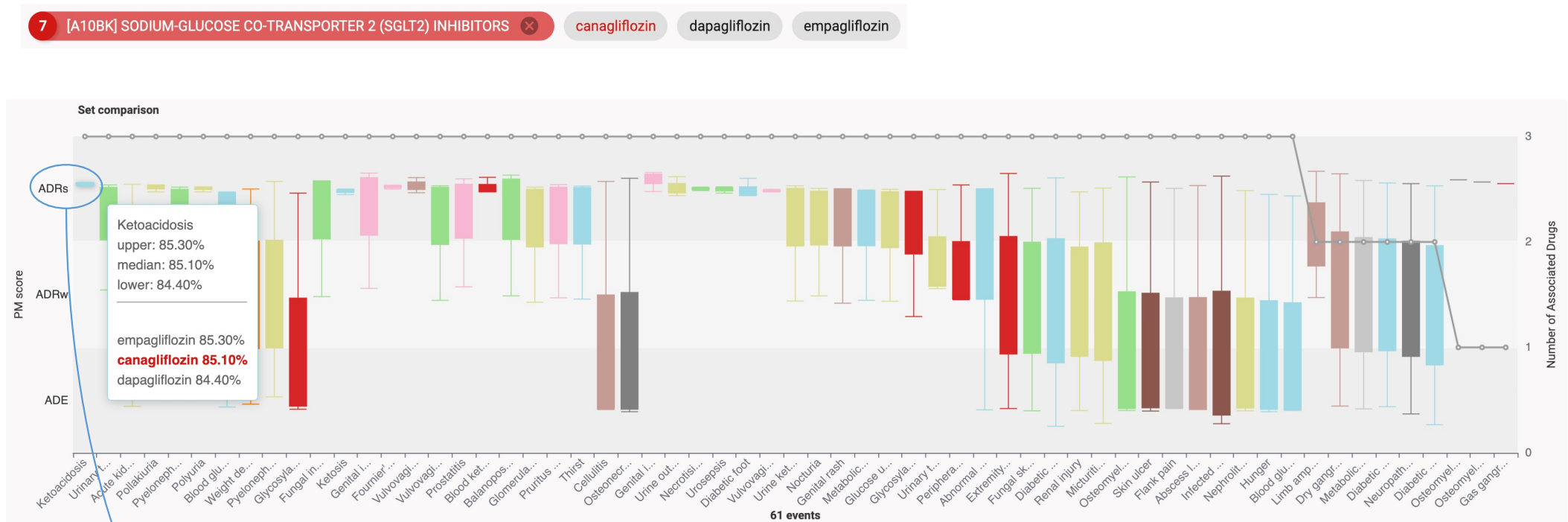
Example: HMGCR inhibitors



**Rhabdomyolysis** is an Adverse Drug Reaction signal (ADRs) for the entire class of HMGCR drugs currently in the market

# Use Case: comparative analyses – class reaction: ketoacidosis

Example: SGLT2 inhibitors



[Ketoacidosis](#) is an Adverse Drug Reaction signal (ADRs) for the entire class of SGLT2 drugs currently in the market

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