evotec

#RESEARCHNEVERSTOPS

E.MPD

TRANSLATIONAL MOLECULAR PATIENT DATABASE

Evotec's Translational Molecular Patient Database (E.MPD)

Dr. Christiane Honisch, SVP EVOgnostic

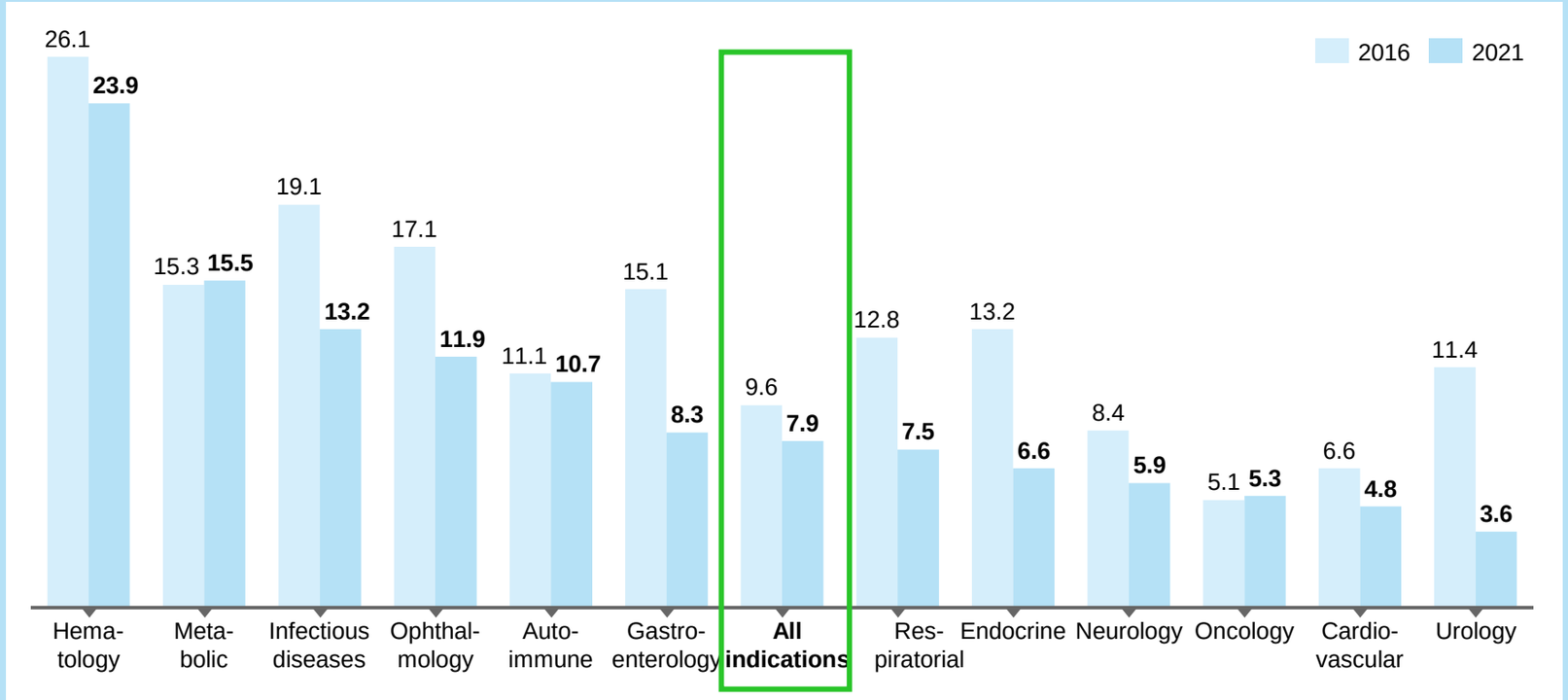
Cautionary statement regarding forward-looking statements

Information set forth in this presentation contains forward-looking statements, which involve a number of risks and uncertainties. All statements other than statements of historical fact are forward-looking statements, which are often indicated by terms such as “anticipate”, “believe”, “could”, “estimate”, “expect”, “goal”, “intend”, “look forward to”, “may”, “plan”, “potential”, “predict”, “project”, “should”, “will”, “would” and similar expressions. The forward-looking statements contained herein represent the judgement of Evotec as of the date of this presentation. Such forward-looking statements are neither promises nor guarantees, but are subject to a variety of risks and uncertainties, many of which are beyond our control, and which could cause actual results to differ materially from those contemplated in these forward-looking statements. We expressly disclaim any obligation or undertaking to release publicly any updates or revisions to any such statements to reflect any change in our expectations or any change in events, conditions or circumstances on which any such statement is based. Given these risks, uncertainties, and other factors, you should not place undue reliance on these forward-looking statements.

Clinical Development Success Rates in Drug Discovery

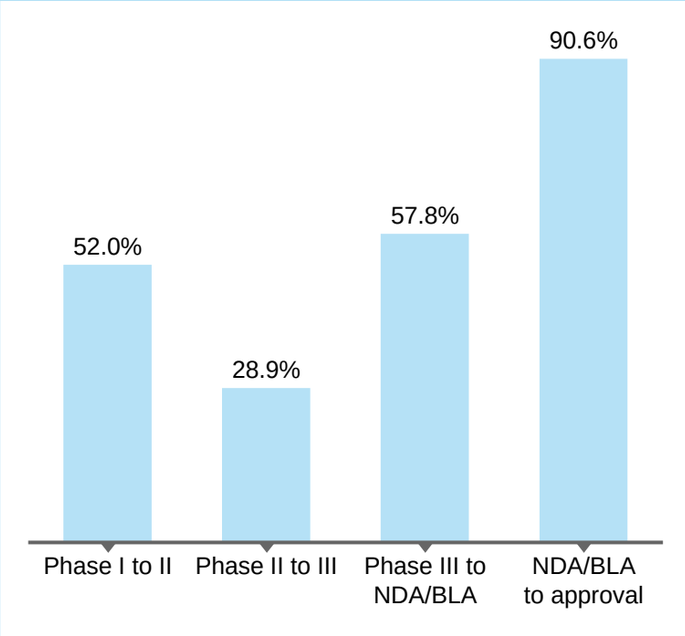
Probability of success on the decline in most indications

Overall clinical success rates in %



Probability of success

success rate = number that advanced to next phase/total number advanced & suspended



Sources: Scrip, Predicting Success: The Easiest, And Hardest Routes To Market, February 2021; BIO, QLS Advisors, Informa UK Ltd: Clinical Development Success Rates and Contributing Factors 2011–2020, February 2021.

Re-defining health and disease

Patient stratification as a starting point for drug discovery

E.MPD
TRANSLATIONAL MOLECULAR PATIENT SAMPLES DATABASE

>200,000 samples | **Billions of data points** | **EVO*panOmics* & EVO*panHunter* & EVO*gnostic*** | **Modality agnostic analysis** | **1st in class treatments**

Patient cohorts

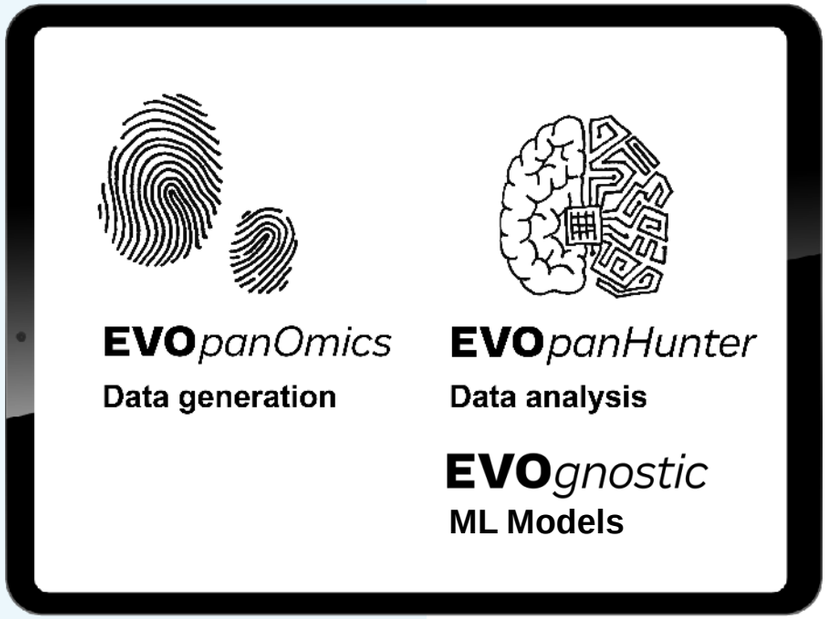
- **Renal diseases**
- **Metabolic disease**
- **Other diseases**
- **Control groups**

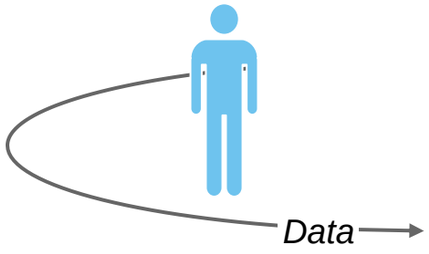
Clinical data

Co-morbidities, Histology, Diagnosis, Organ function, Blood chemistry, Anthropomorphic

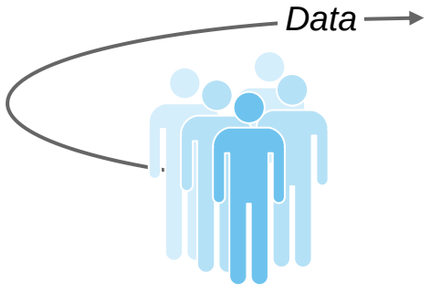
Omics data

sc/snRNA-Seq, Transcriptomics, Proteomics, Metabolomics, Exome Seq, SNPs





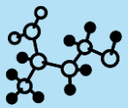
Accurate patient stratification



Transform clinical trial design & execution

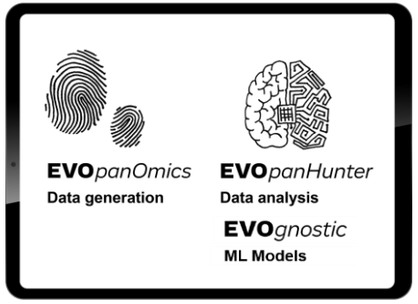
Biological insights enable precision medicine

Transcriptomics and proteomics provide more biological insight than genomics

	Robustness	Scalability	Cost efficiency	Biological insight
Genomics 				
Transcriptomics 				
Proteomics 				
Metabolomics 				
	Reproducibility • Day to day • Month to month • Year to year	Throughput • High • Medium • Low	Cost efficiency • High • Medium • Low	Molecular insights in • Cause of disease • Manifestation of disease • Organs, tissues, cells

EVO*panOmics*

High Performance Transcriptome and Proteome



Genomics	Standard process
ScreenSeq **Transcriptomics**	**High Performance Transcriptomics** • **Unprecedented throughput and sequencing depth**
ScreenPep **Proteomics**	**High Performance Proteomics** • **Unprecedented scale and protein coverage**
Metabolomics	Standard process

Predictive drug discovery – Evolving paradigm

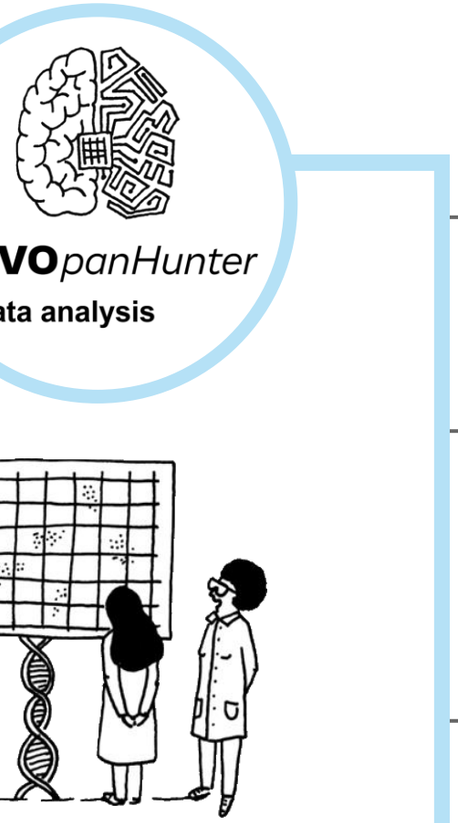
- Seamless and cost effective platforms and processes
- AI/ML driven data analytics
- Connecting patient disease profiles to compound profiles

EVO*panHunter*

Easy access to complex data analysis – connecting complex clinical and pre-clinical data

Omics data
- Transcriptomics
- Genomics
- Proteomics
- Metabolomics

Clinical data
- Demographic information
- Medication
- Comorbidities



Meta data
- Gene/protein information
- Experimental parameters

Chemical data
- Structures
- Compound information
- Drug databases

More data
- Public knowledge
- BioMol databases, e.g. Wikipathways

We integrate AI/ML throughout the value chain

AI/ML driven drug discovery and patient stratification

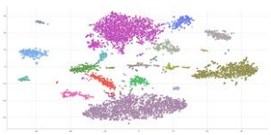
Target ID/ validation | **Hit identification** | **Lead optimisation** | **Pre-clinical tox testing** | **INDiGO** | **Phase I** | **Phase II** | **Phase III** | **Market**

Multi-omics data analytics and compound profiling along the full value chain

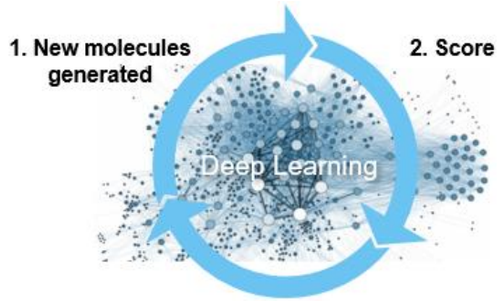
EVO*gnostic*

(AI/ML derived signature generation)

AI/ML supported cell type annotation



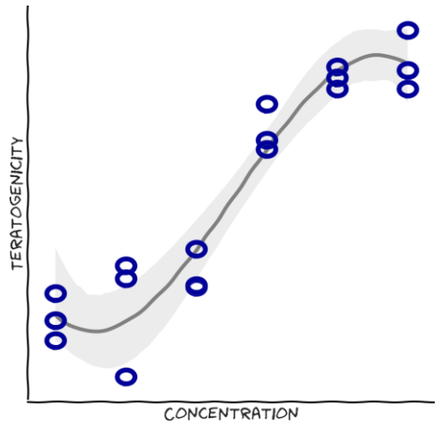
Generative design[1)]



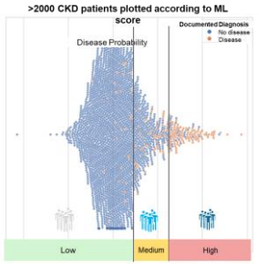
J.HAL℠ JUST – EVOTEC BIOLOGICS | J.DESIGN | E.INVENT-AI MOLECULAR DESIGN EXCELLENCE

Safety prediction

70% → 86% prediction improvement - DILI platform[2)]



Patient stratification

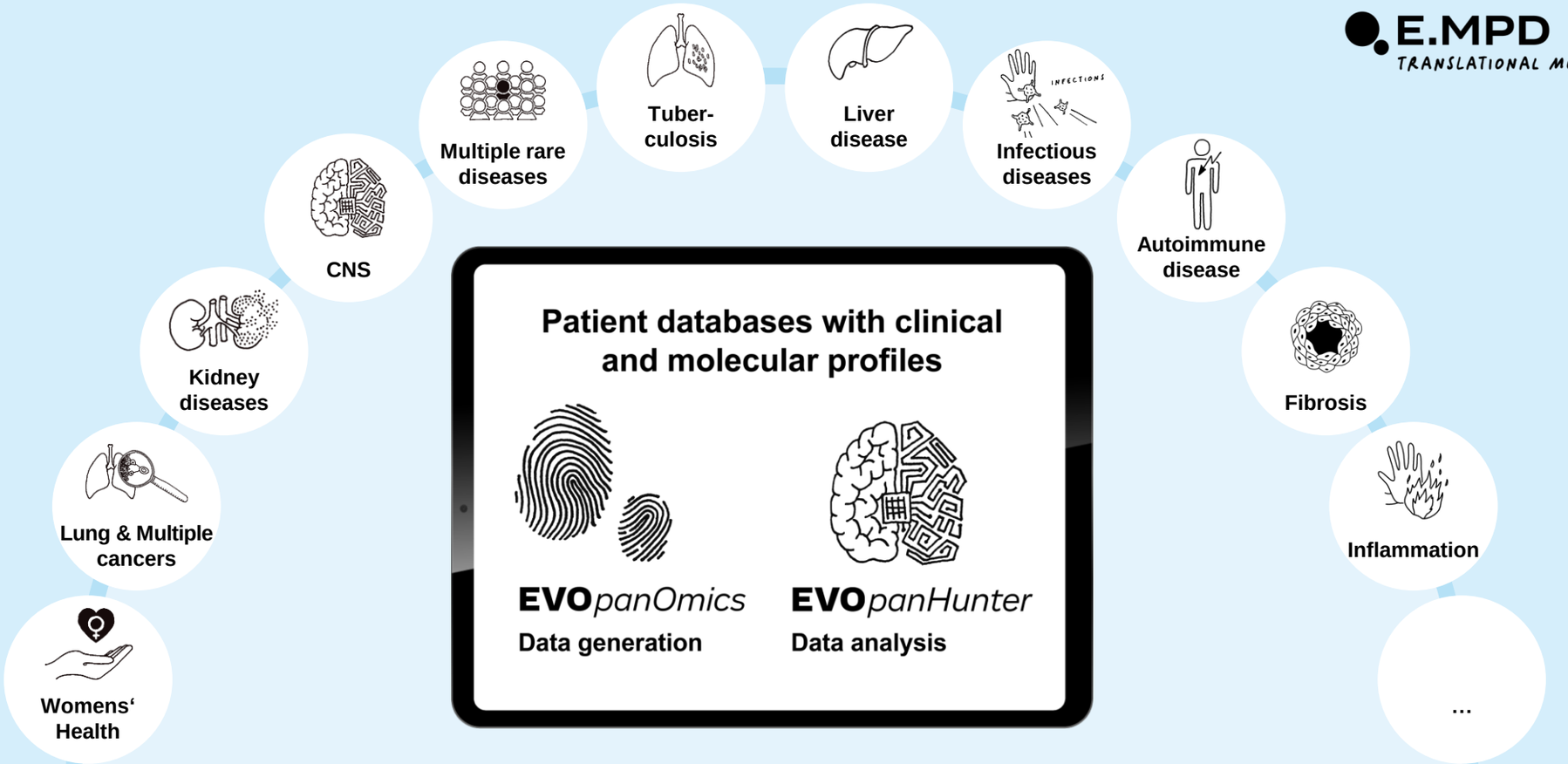


[1)] J.HAL is a GAN based AI-driven discovery platform, producing diverse human antibodies with broad efficacy features biased toward developability

[2)] Prediction are based on 2D Primary Human Hepatocyte assay with 128 reference compounds tested (largest reference compound data base reported), HCI: High content imaging, DILI: Drug induced liver injury

Deep understanding of biology for precision medicine

The Evotec Molecular Patient Database (E.MPD)



EVO*panOmics*: Genomics, Transcriptomics, Proteomics and Metabolomics
EVO*panHunter*: Bioinformatics, AI/ML

Fast growing unique human data source

The Evotec Molecular Patient Database (E.MPD) in numbers

# of patients

15,000+

# of samples

200,000+

# of data points generated so far

200 bn+

# of searchable data categories per patient in the E.MPD

50-500

# of clinically described diseases / etiologies in the E.MPD

30+/100+

# of targets from E.MPD in target validation & drug discovery

30+

Globally leading in kidney diseases

Overview/Example: >12,000 participants; >3,000 kidney biopsies

2018	2019	2020	2021	2022
• CKD & NephSyn • ~ 4,000 patients • ~ 900 kidney biopsies • Blood, serum & urine samples • Clinical records	• CKD (SKS) • ~ 2,000 patients • ~ 250 kidney biopsies • DNA, serum samples • Clinical records	• Healthy controls • 1,000 patients • 2,500 tissue biopsies • Kidney, liver, heart, serum • Clinical records	• CKD • ~ 5,000 patients • ~ 800 kidney biopsies • Blood, serum & urine samples • Clinical records	• NephSyn • ~ 300 patients • ~100 kidney biopsies • DNA, blood samples • Clinical records

https://www.nurturebiobank.org/
https://www.hra.nhs.uk/planning-and-improving-research/application-summaries/research-summaries/salford-kidney-study/
https://www.gckd.de/; https://quod.org.uk/

SKS: Salford Kidney Study (CRISIS)
NURTuRE: National Unified Renal Translational Research Enterprise

CKD: Chronic kidney disease
NephSyn: Nephrotic Syndrome
QUOD: Quality in Organ Donation

Significant advantages over public domain data sets

Standard technology, data QC and rich data annotations to improve outcomes

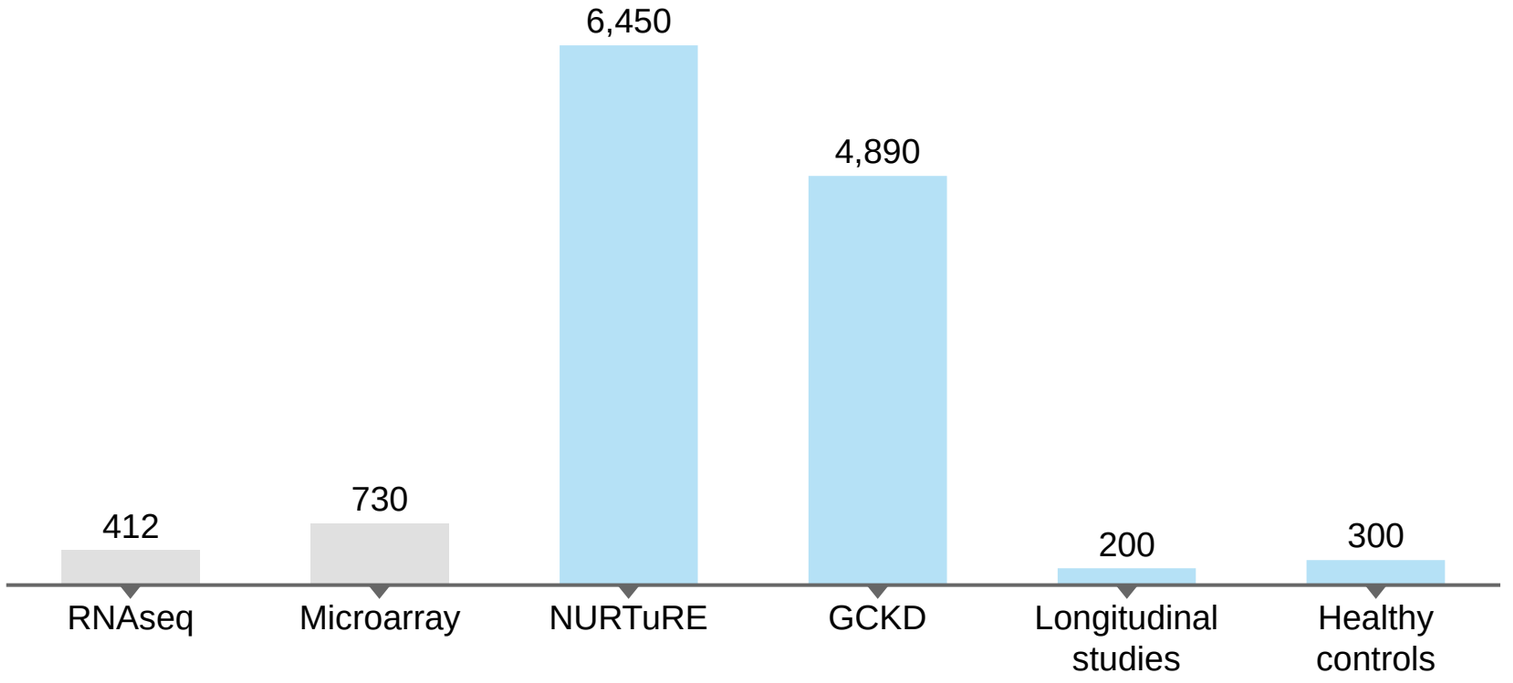
		Public Domain	E.MPD TRANSLATIONAL MOLECULAR PATIENT DATABASE
Cohort planning/design	Physician engagement	○	●
	Prospective and longitudinal studies	◔	●
Clinical data	Sample ID linked to source data (e.g. hospital)	○	●
	Sample tracking (batch effects!)	○	◕
	Medical records	○	◕
	Evotec QC of medical record data	◔	●
	Number of annotations (age, sex, medication, comorbidities, …)	1-5	50-500
Analysis data	OMICS technology platform	several, no control	one, fully validated
	Availability of multi-omics data sets	◔	◕
	Data acquisition (sensitivity, sequencing depth, …)	◑	●
	Data comparability (combining cohorts)	◔	●

World leading in blood transcriptomics

Deep insights into kidney disease

- E.MPD NURTuRE and GCKD cohorts for blood transcriptomics are unique in kidney disease:
  - by far highest sample numbers
  - extensive clinical data
  - most comprehensive molecular profiling based on blood transcriptomics
- No large-scale blood transcriptomic studies in the public domain

Blood transcriptomics at Evotec, # of blood samples

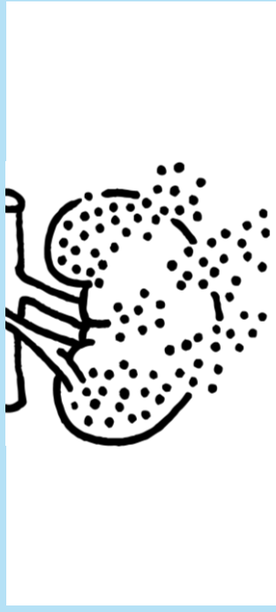


Public domain Evotec

High quality data sources for increased probability of success

Superior signal-to-noise ratio on Evotec data compared to public domain data sets

Kidney cohorts



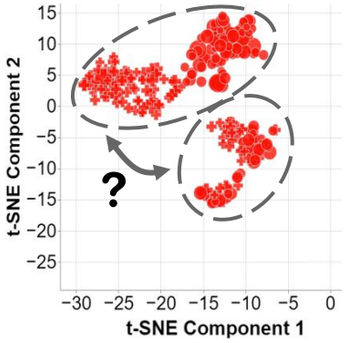
Cohort information and medical records

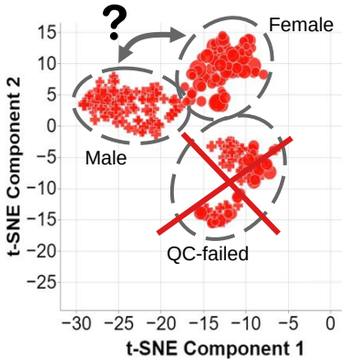
Public domain data

- No data QC info
- < 10 annotations
- No batch info

E.MPD TRANSLATIONAL MOLECULAR PATIENT DATABASE

- Data QC
- > 50 annotations
- Batch information





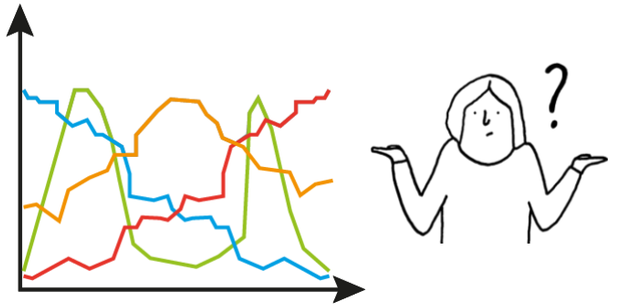
OMICS / sequencing data

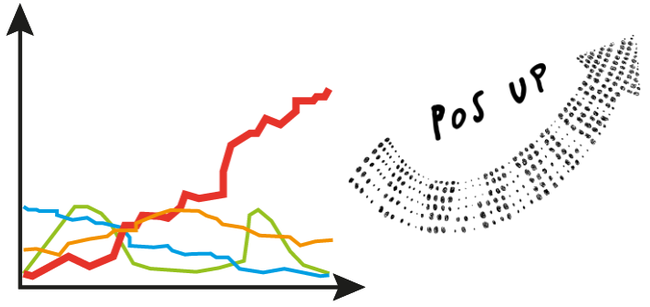
Public domain data

- Several platforms
- One read out
- No batch info

E.MPD TRANSLATIONAL MOLECULAR PATIENT DATABASE

- 1 platform, QC
- Multi-omics
- No batch effects



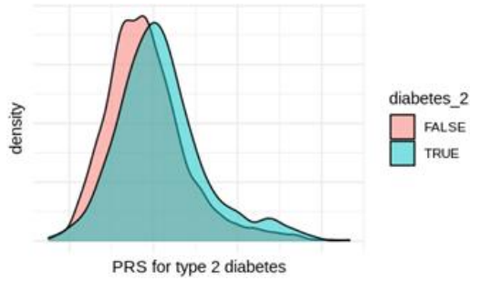


Molecular profiling leads to deep understanding of diseases

Multi-omics analysis on patient samples

SNP analysis (DNA)

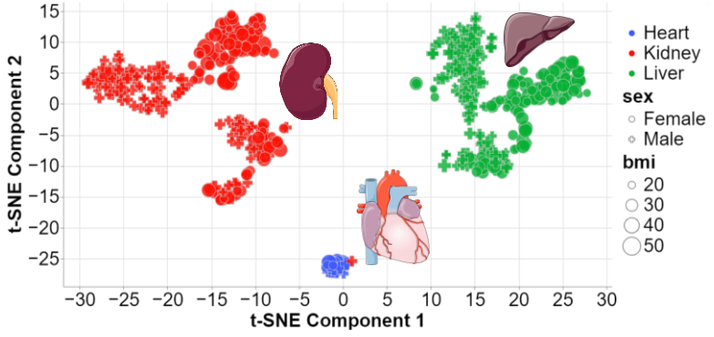
Polygenic risk score based on DNA analysis



Polygenic risk score estimating genetic predisposition for diabetes type 2

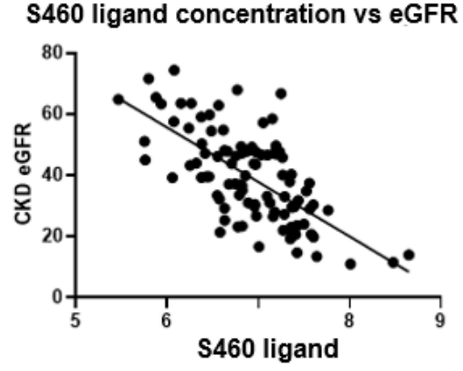
Transcriptomics (mRNA)

RNA sequencing to identify key driver and mechanisms of diseases



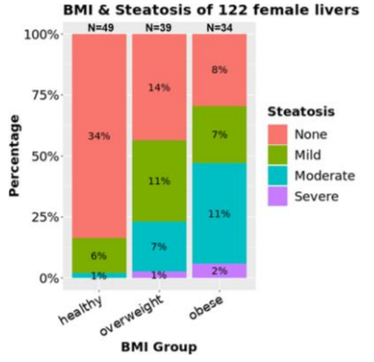
Proteomics (Proteins)

Proteomics analysis to confirm key mechanism on protein level



Clinical parameter

Integration of clinical records and histology



World-leading in high-throughput transcriptomics & proteomics processing and analysis

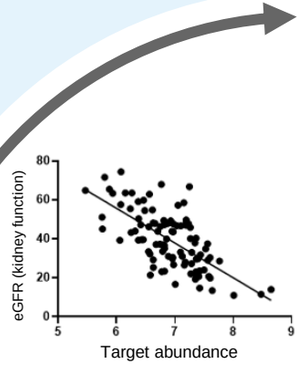
From bedside to bench and back to bedside

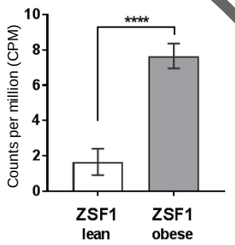
Example: Human target ID

1

Patient serum proteomics analysis

Negative correlation of target abundance to kidney function (eGFR) in CKD patient serum

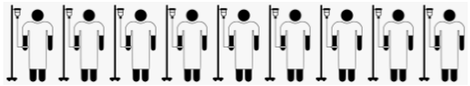




Rodent kidney transcriptomics

Healthy vs diseased rats: Target strongly up-regulated during disease

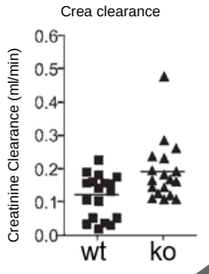
2



3

Kidney function

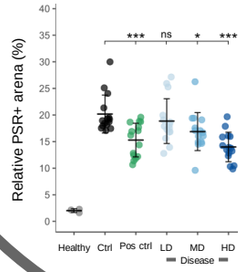
Knock-out mice with significantly improved kidney function in CKD



4

***In vivo* efficacy with therapeutic inhibitor**

Small molecule inhibitor suppresses kidney fibrosis in CKD



CKD: Chronic Kidney Disease
DKD: Diabetic Kidney Disease
KO: Genetic target knock out

E.MPD core component of alliances in CKD

CKD strategic drug discovery deals – "…just the beginning"

2016/17	2018/19	2020	2021	2022
• Upfront • Research funding • Milestones > € 300 m per product • Tiered royalties	• Vifor funded: € 25 m • 50% on all projects	• Upfront • Research funding • Milestones > € 150 m per product • Tiered royalties	• Upfront • Research funding • Milestones • Tiered royalties	• Upfront • Research funding • Milestones US$ 180 m per product • Tiered royalties

From Target identification & validation, via biomarker identification, to patient stratification

Accelerating changes in the healthcare paradigm

Omics based patient stratification, disease prevention and early intervention

Established diagnostics paradigm

Patient sees doctor only with symptoms

Doctor exams patient and makes initial diagnosis

Follow-up diagnostic tests (blood, urine)

Disease specific diagnostics

- Imaging
- Biopsy
- Histology

Too late Interventions

- Life style changes
- Medication and therapy
- Surgical interventions

Intervention
Disease Management

Omics driven personalised disease monitoring in the future

Healthy subjects with regular health checks

Health stratification by blood transcript-omics & AI/ML

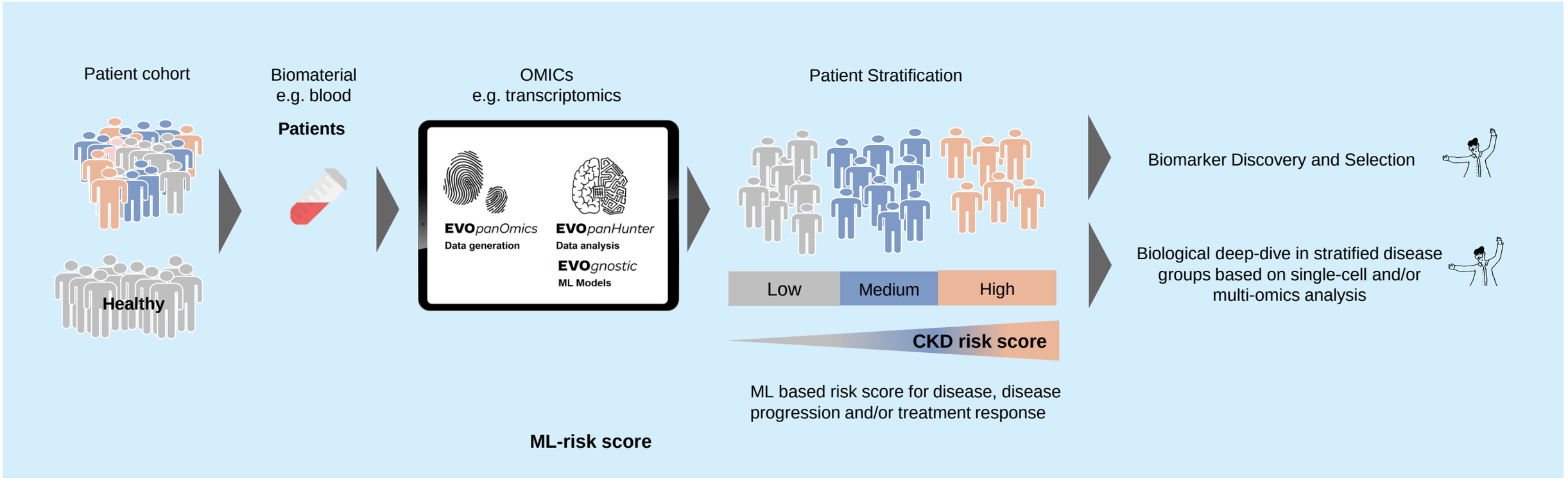
Early detection of pre-dispositions and latent disease

- Disease prevention
- Less invasive treatment and Life style changes
- Prolonged life expectancy

Prevention - Health Management

EVO*gnostic* patient stratification, disease and treatment monitoring

A new way to define patient populations



E.MPD TRANSLATIONAL MOLECULAR PATIENT SAMPLES DATABASE

EVO*panOmics*

EVO*gnostic*

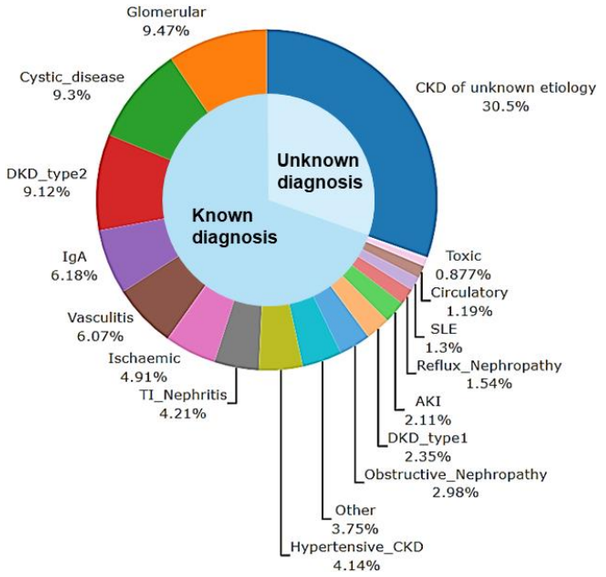
EVO*gnostic* learning models (AI/ML) in kidney disease

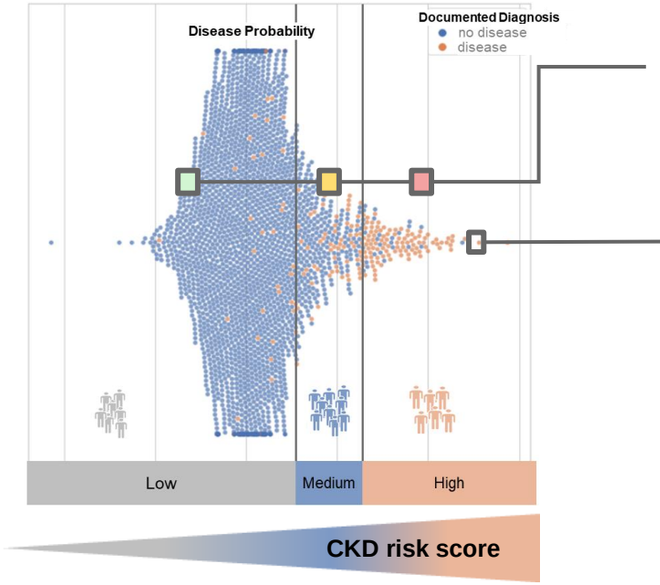
Patient stratification and personalized disease monitoring

NURTuRE – patient cohort

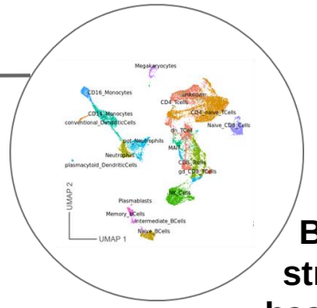
>2,000 CKD patients plotted according to CKD risk score

Diagnostic Markers
Disease Insights





Biomarker Discovery and Selection



Biological deep-dive in stratified disease groups based on single-cell and/or multi-omics analysis

Todays diagnostics paradigm of complex diseases, will be replaced by OMICS test

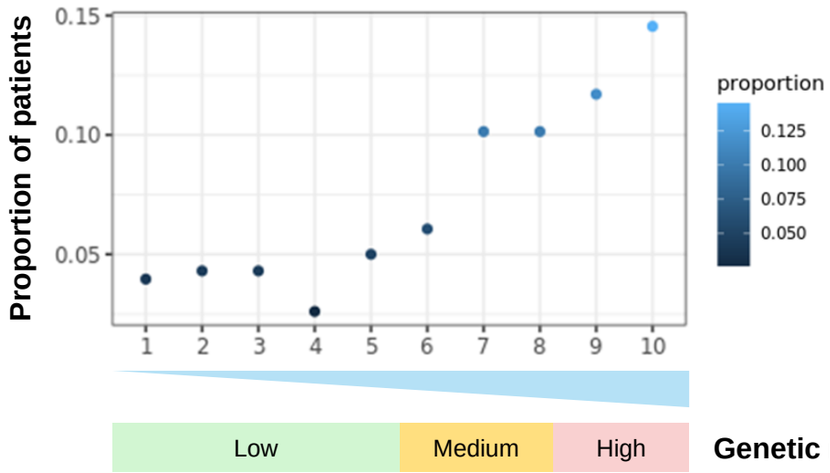
CKD: Chronic kidney disease

Genetic predisposition adds an additional layer for prevention

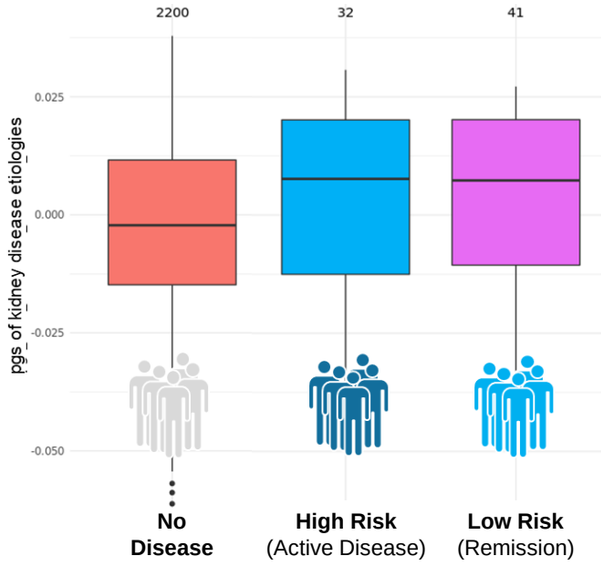
Predisposition for disease/phenotype based on genetics

Genomics

Genetic predisposition determined for >5,000 CKD patients



Patients with genetic predis-position show higher risk of developing disease



Genetic predisposition combined with CKD risk score to increase diagnostic test precision

Source: PGS (polygenic risk score) Catalog – https://www.pgscatalog.org/; GWAS Catalog – https://www.ebi.ac.uk/gwas/

E.MPD expansion will accelerate multiple therapeutic areas

Selected key events to watch out for

E.MPD
TRANSLATIONAL MOLECULAR PATIENT DATABASE

"Evotec's Translational Molecular Patient Database (E.MPD) re-defines patient populations according to disease mechanisms rather than symptoms. This paves the way for true precision medicine"

Kidney diseases

- Access to selected kidney disease etiologies
- Prospective longitudinal studies
- Pre-disease / early stage disease cohorts

Liver disease

Inflammation

Fibrosis

- Access to NAFLD, NASH & liver fibrosis patient cohorts
- Add metabolic disease / diabetes cohorts
- Access to inflammatory & autoimmune disease cohorts

Oncology

Neuro-inflammation

Infectious Diseases

- Access to samples and data in the oncology & neuroinflammation space
- Studies for effective treatment monitoring in tuberculosis
- Cohort studies to understand and conquer Long COVID

Evotec‘s Molecular Patient Database

Evotec’s Precision Medicine platform brings disease more relevance into drug discovery

E.MPD
TRANSLATIONAL MOLECULAR PATIENT DATABASE

- **Patient data** are instrumental for a better understanding of disease etiologies.
- The **EVOpanOmics platform** generates comprehensive high quality Omics data.
- **EVOpanHunter** connects OMICs with complex clinical data.
- Evotec employs **machine learning** in all aspects of patient stratification, drug discovery and development.
- Indepth molecular profiling of patient **cohorts** is constantly feeding the E.MPD.
- The **E.MPD** expansion will accelerate multiple therapeutic areas

evotec

#RESEARCHNEVERSTOPS

QUESTIONS AND ANSWERS