

# CENTOGENE

THE RARE DISEASE COMPANY

Diagnose.  
Understand.  
Treat.

Investor & Analyst Event  
June 2021



## Speakers and agenda

### 1. Strategy Update

Andrin Oswald | CEO



### 2. Building the Leading Bio/Databank in Rare Diseases

Bettina Goerner | CDO



### 3. Superior Genomics Insights for Clinical Diagnostics

Max Schmid | CCO Dx, Peter Bauer | CGO



### 4. Enabling Differentiated Orphan Drug Development

Michael Motz | CCO Pharmaceuticals, Justin Bingham | SVP Business Development



### 5. Unlocking the Complexity of Rare Diseases With Multiomics

Volkmar Weckesser | CIO, Claudia Cozma | VP Biomarker, Philip Lambert | CSO



### 6. Finance Priorities and Process Optimization

Rene Just | CFO<sup>1</sup>



## Safe harbor statement

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For further information, please refer to the Risk Factors section in our Annual Report for the year ended December 31, 2020, on Form 20-F filed with the SEC on April 15, 2021 and other current reports and documents filed with the U.S. Securities and Exchange Commission (SEC). You may get these documents by visiting EDGAR on the SEC website at [www.sec.gov](http://www.sec.gov).



# 1 • Strategy Update

# If it is rare, I care

Andrin Oswald, M.D.



Schweizerische Eidgenossenschaft  
Confédération suisse  
Confederazione Svizzera  
Confederaziun svizra



ICRC

McKinsey  
& Company



BILL & MELINDA  
GATES *foundation*

## Why rare?

We focus on rare diseases, one of the highest unmet patient need areas remaining and a large and growing market



**~350 Million** people  
affected by rare genetic diseases, ~90% undiagnosed.

**<5%** of rare diseases have meaningful  
therapies, ~7,000 hereditary rare diseases identified.

Market is accelerating in terms of sales as well as R&D spend

Market for therapies and diagnostics in rare diseases is growing

## Orphan Drug Market



2016



2021

with CAGR of

~11%

# Precision medicine at the focal point of technology and therapy trends

Enabled by access to real world patient data



AI and big data empowering the analysis of complex datasets

Precision medicine for genetically driven diseases is enabled by technological development in recent years.



Breakthrough new therapeutic platforms gaining ground e.g., Gene, RNA, and cell therapy, CRISPR



Multiomics tools accelerating the medical revolution



# Mission

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We are a data-driven rare disease company that unlocks the complexities of patients' biology to diagnose, understand, and treat rare diseases.

Our goal is to enable the cure of 100 rare diseases in 10 years.



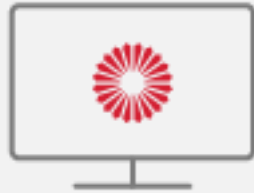
# What makes CENTOGENE unique?

Bridging the gap between strong technology trends and new therapy platforms

## Precision medicine for genetically driven diseases is in our DNA.



Leading genomic rare disease **expertise**



Strong **brand** in scientific and medical community



Largest **Bio/Databank** with samples of rare genetic diseases



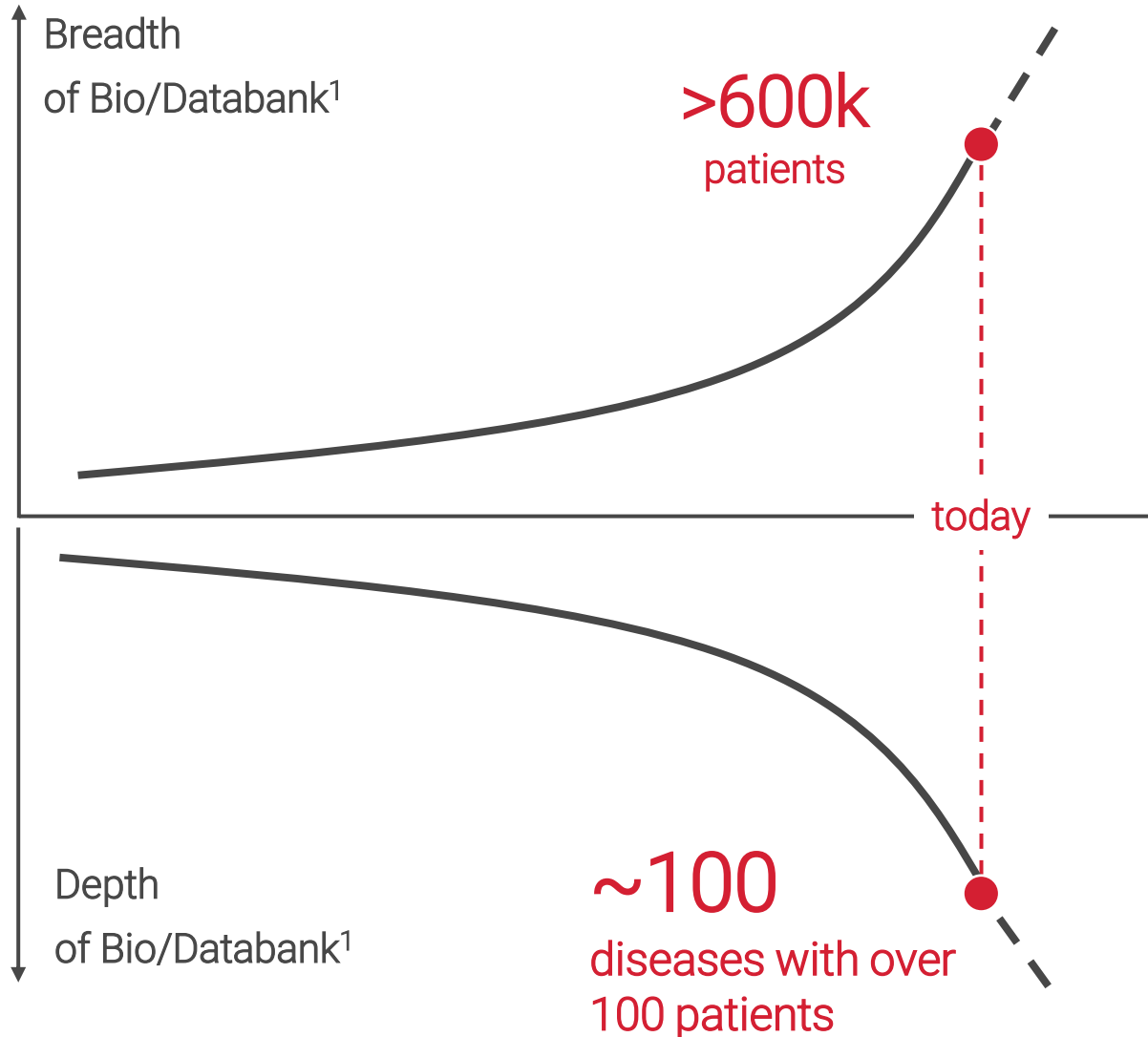
Global **footprint** incl. many countries where rare genetic diseases are highly prevalent



Strong, established **physician** and customer network

# Unique and fast-growing Bio/Databank for rare diseases

Every diagnosed patient improves our position to enable discovery, development, and translation



## Breadth of Bio/Databank



Geographical diversity of samples allows us to generate unique insights

## Depth of Bio/Databank



Insights into genotype/phenotype associations



Connecting patients to develop disease-specific knowledge













Full disease models driving new therapies

<sup>1</sup> Illustrative graphs. Metrics dependent on exact definition incl. variant classification.

# Leading data-driven insights creator in rare diseases

Peer group of data-driven insights companies

|                                                                                                                  |  | <b>TEMPUS</b> |  | SEMA4 | insitro |  |  |
|------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------|---------------|-------------------------------------------------------------------------------------|-------|---------|-------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------|
|  Focus on rare diseases         | ✓                                                                                   | ✗             | ✗                                                                                   | ✓     | ✓       | ✓                                                                                   | ✗                                                                                   |
|  Databank                       | ✓                                                                                   | ✓             | ✓                                                                                   | ✓     | ✓       | ✓                                                                                   | ✓                                                                                   |
|  Biosamples                     | ✓                                                                                   | ✓             | ✓                                                                                   | ✓     | ✗       | ✓                                                                                   | ✗                                                                                   |
|  Proprietary data value chain   | ✓                                                                                   | ✓             | ✓                                                                                   | ✓     | ✓       | ✓                                                                                   | ✓                                                                                   |
|  Geographical diversity       | ✓                                                                                   | ✗             | ✓                                                                                   | ✗     | ✗       | ✗                                                                                   | ✗                                                                                   |
|  Multiomics & multimodal data | ✓                                                                                   | ✓             | ✓                                                                                   | ✓     | ✓       | ✗                                                                                   | ✓                                                                                   |

Reflecting internal assessment. Legend: ✓ fully, ✓ partially, ✗ minor/none

## Newly-formed leadership team focused on value creation

### Building the Leading Bio/Databank in Rare Diseases

Bettina Goerner | Chief Data Officer



### Superior Genomics Insights for Clinical Diagnostics

Max Schmid | CCO Dx, Peter Bauer | Chief Genomic Officer



### Enabling Differentiated Orphan Drug Development

Michael Motz | CCO Pharmaceuticals, Justin Bingham | SVP Business Development



### Unlocking the Complexity of Rare Diseases With Multiomics

Volkmar Weckesser | CIO, Claudia Cozma | VP Biomarker, Philip Lambert | CSO



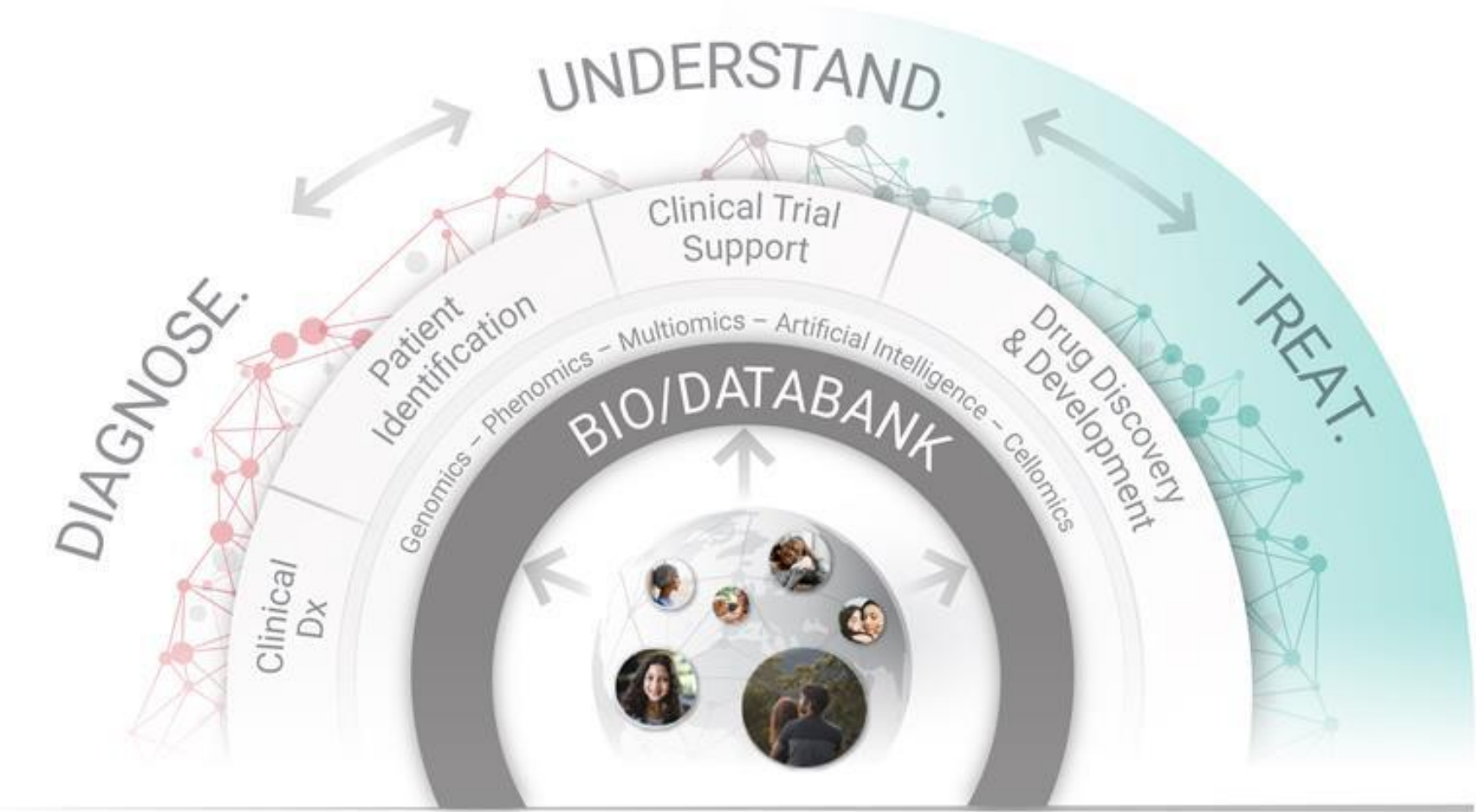
### Finance Priorities and Process Optimization

Rene Just | CFO<sup>1</sup>



<sup>1</sup> To be appointed at upcoming AGM

# CENTOGENE business model and strategic value creation

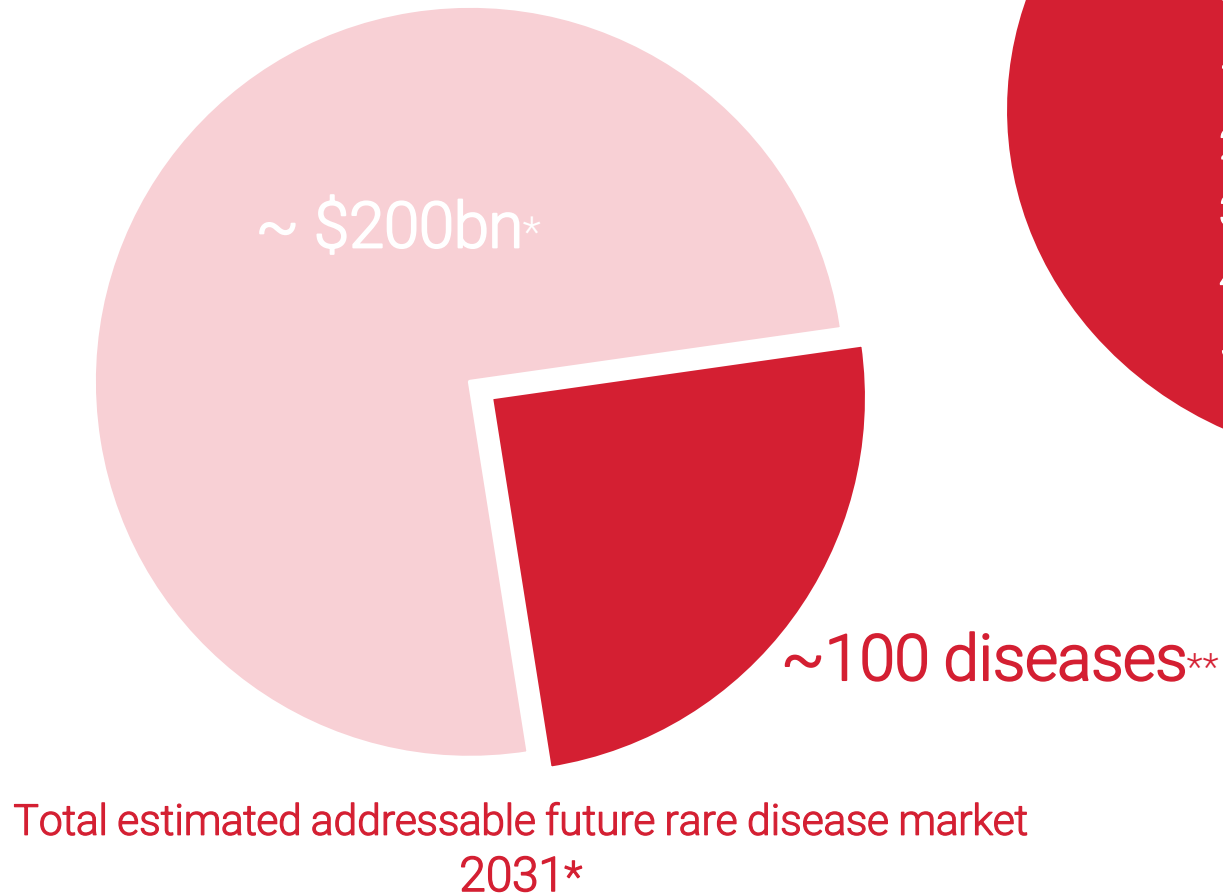


# Tremendous future value potential for CENTOGENE by enabling orphan drug development

Future potential of capturing share of orphan disease market

## CENTOGENE Key levers

- > Superior patient diagnostic insights
- > Accelerate clinical trials
- > De-risk clinical trials
- > Increase chance of approval
- > Maximize re-imbursement



## Estimated annual royalty revenue potential \*\*\*

- 1% ≈ \$ 0.5 billion
- 2% ≈ \$ 1.0 billion
- 3% ≈ \$ 1.5 billion
- 4% ≈ \$ 2.0 billion
- 5% ..

\*Above represents CENTOGENE's internal estimates based on the total orphan drug market of \$156bn in 2021 by Evaluate Pharma® February 2020, estimating the addressable non-oncology rare disease market at ~\$70bn in 2021 and applying the CAGR of 11% for 10 years, leading to an estimated future rare disease market potential of ~\$200bn in 2031.

\*\*Future market potential estimate based on peak sales of \$500M per orphan drug for 100 diseases.

\*\*\* Estimated annual revenue potential from potential future royalty share calculated on the basis of the estimated future rare disease market potential 2031.

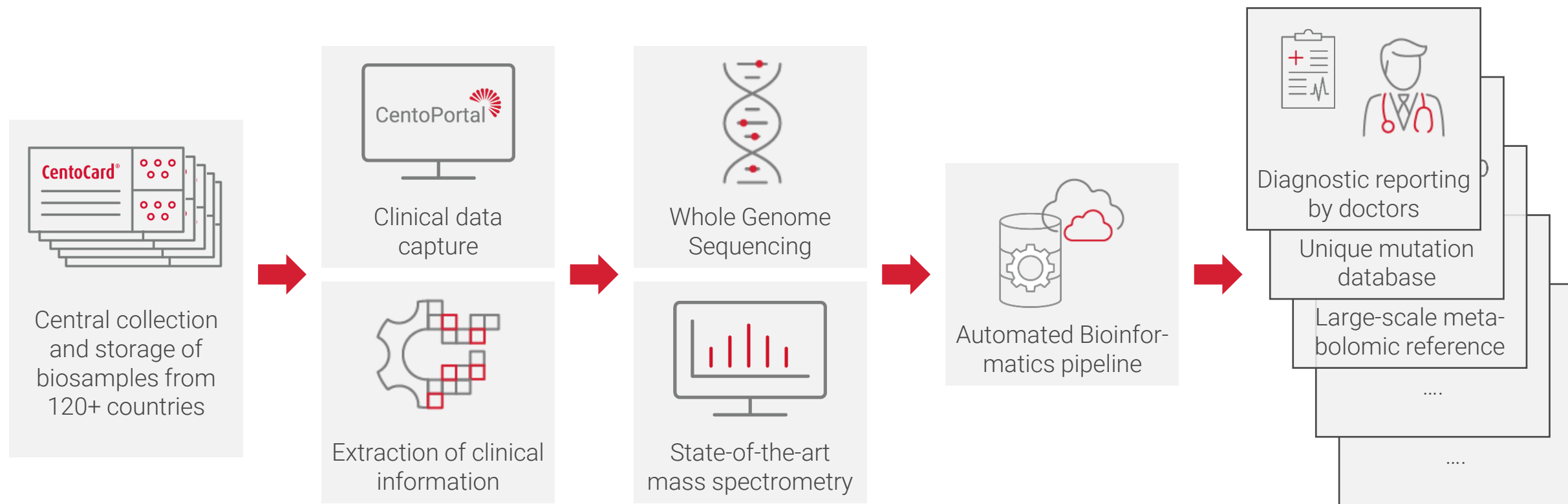


# 2. Building the Leading Bio/Databank in Rare Diseases



# Samples from all over the world proceed along our cutting-edge value chain

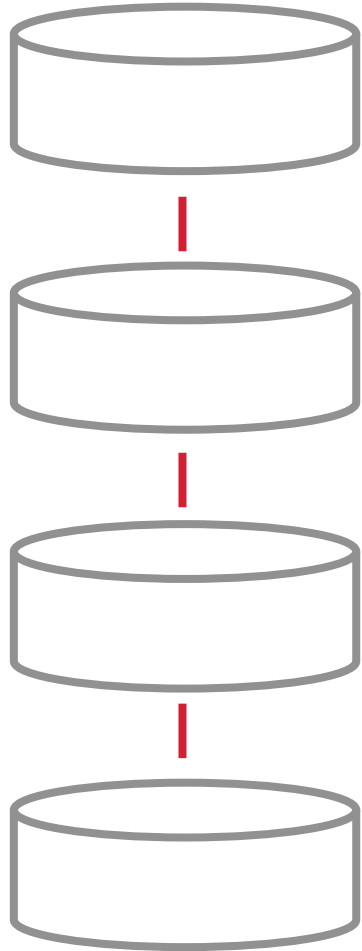
Data capture, processing, and analysis is fully owned by CENTOGENE and is optimized for value generation



*Value chain supported by advanced bioinformatics and AI tools*

# What data do we have?

Our multi-modal data is rich with clinical and biological insights



## Biomaterial & Extracts

Dried Blood Spots cards



## Sociodemographic Information

Age, geography



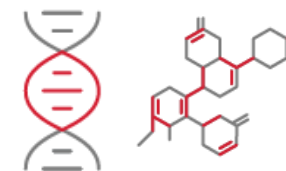
## Clinical Information

For Parkinson's: Age of onset, motor and other symptoms, comorbidities, treatment, etc.



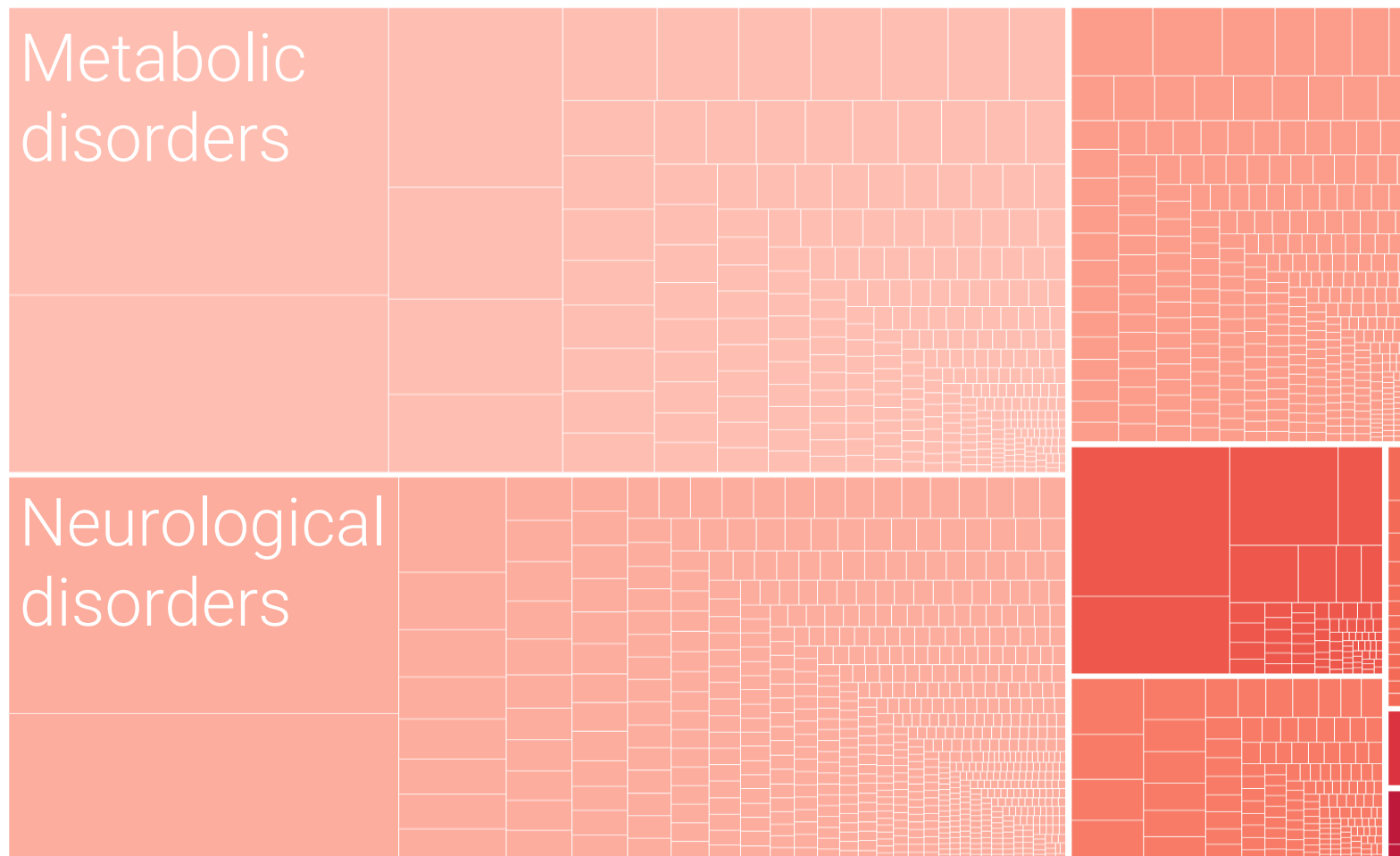
## Multomic Data

For Parkinson's: Parkinson's core genes and panel; Whole Genome Sequencing & biomarker data



# Our data from genetically diagnosed patients covers >2,500 diseases

Strength in metabolic & neurological (CNS) disorders

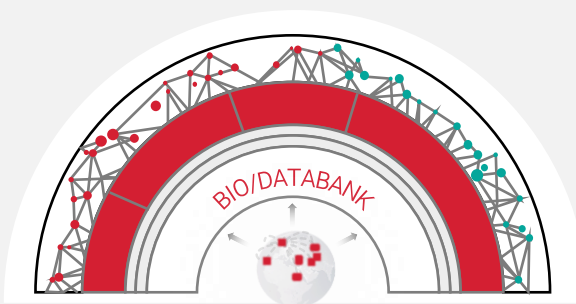


**Hierarchical data** structure of genetically diagnosed patients and related diseases

Each color represents each **disease group**. Each subcategory within the same color represents the specific disease.

The size of the subcategory corresponds to the **proportion of patients** in this disease group.

## Our growing Bio/Databank enables key use cases with data breadth & depth



Clinical Dx

**>2,500**  
rare diseases diagnosed to date

Patient Identification

**>31** million  
unique variants

Clinical Trial Support

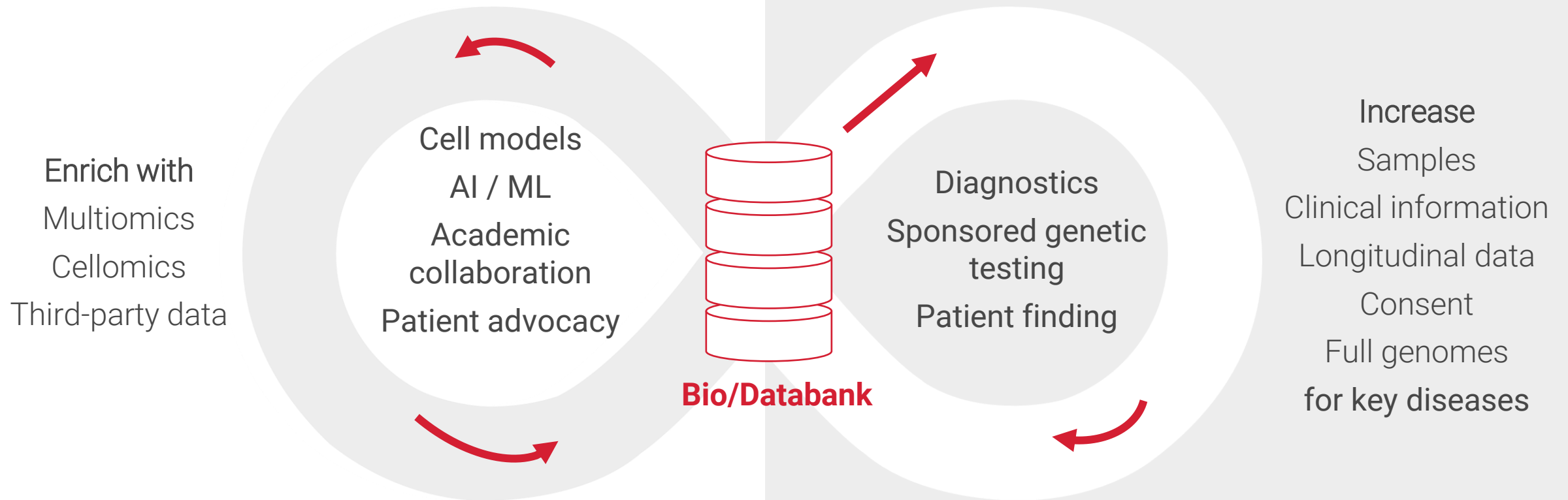
**>300**  
disease cohorts with at least 20 patients

Drug Discovery &  
Development

**>400,000**  
biosamples  
**20,000**  
physicians in our network w/ contact in last 5 years

**Progress full disease models**  
each ~100-500 diagnosed patients with full-omics profile and ~10-20 cell lines for the cellular model in growing number of full disease model

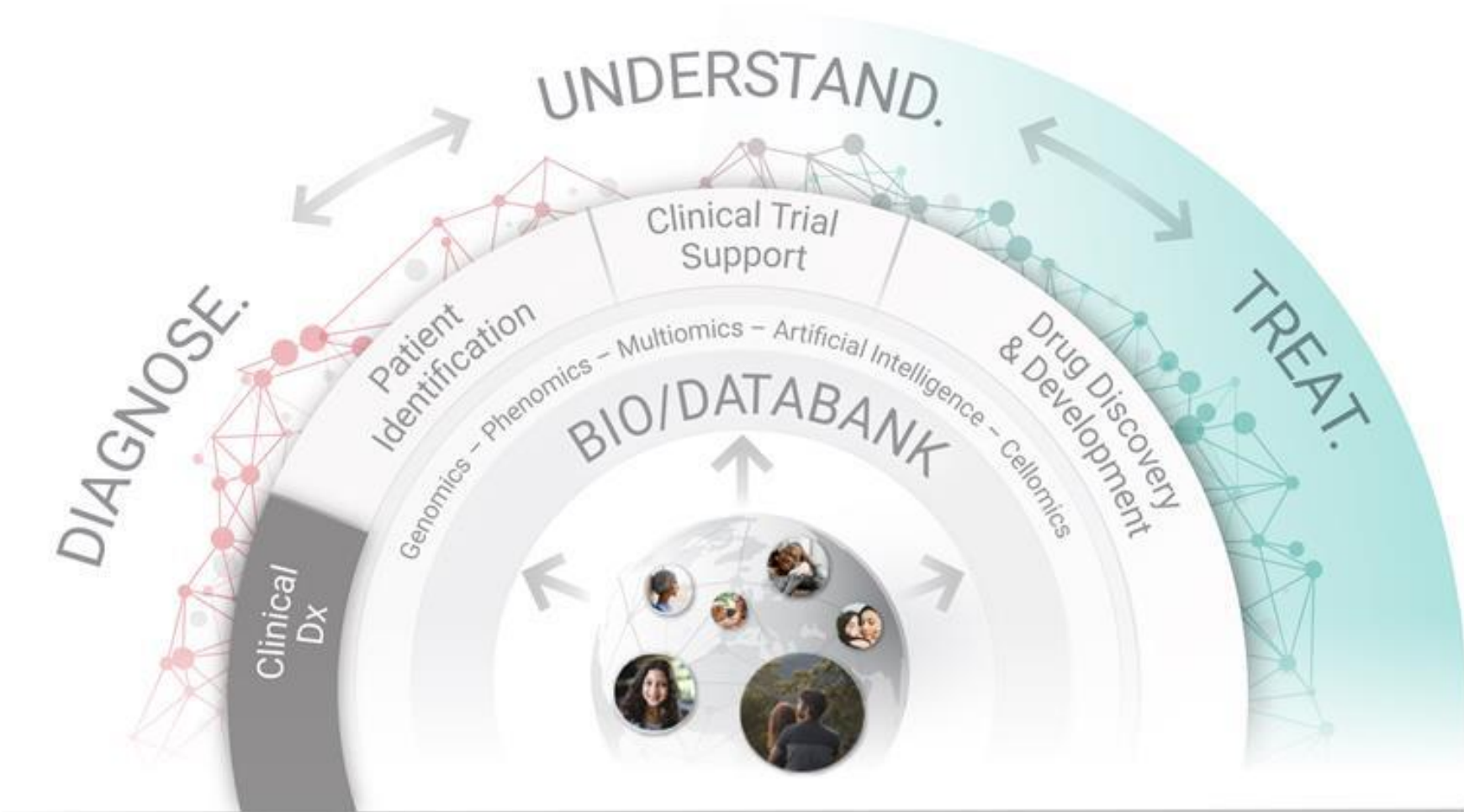
# We manage our Bio/Databank flywheel proactively to grow best-in-class datasets for diseases





# 3. Superior Genomics Insights for Clinical Diagnostics

# CENTOGENE business model and strategic value creation



## Superior genomic insights for diagnosing rare diseases

We are a recognized worldwide leader in rare disease diagnostics with 15 years of experience and a unique Bio/Databank

### Our Unique Strength



Our **distinctive product offering** is centered around high quality genetic testing to diagnose rare genetic diseases



We have a **strong presence** in and good access to countries with a **high prevalence of rare diseases**



Our CentoCard<sup>®</sup> provides **easy logistics** for central testing



Our diagnostic solutions are powered by our unique, proprietary Bio/Databank – enabling us to generate **best-in-class medical insights**



We are capitalizing on the increasing shift to Next Generation Sequencing as a first-line tool in clinical practice and **rapid market growth**



CENTOGENE has been an early proponent of Dx Whole Genome Sequencing

Scientific developments are award-winning

*“Successful application of genome sequencing in a diagnostic setting: 1,007 index cases from a clinically heterogeneous cohort”*

**Abstract**



2020 EJHG  
Reader’s Choice



2020 EJHG  
Editor’s Choice

# Genotype and phenotype connections driving diagnostic yield

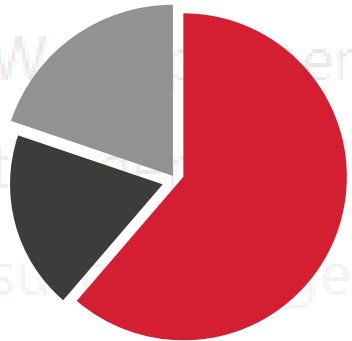
A Dx success story in Pakistan

*“Genomic testing in 1,019 individuals from 349 families results in high diagnostic yield and clinical utility”* npj | genomic medicine

# 51.9%

of diagnosed patients have new or adjusted treatment implemented

## Abstract



# 61.3%

GENETIC DIAGNOSIS  
(P/LP VARIANTS)



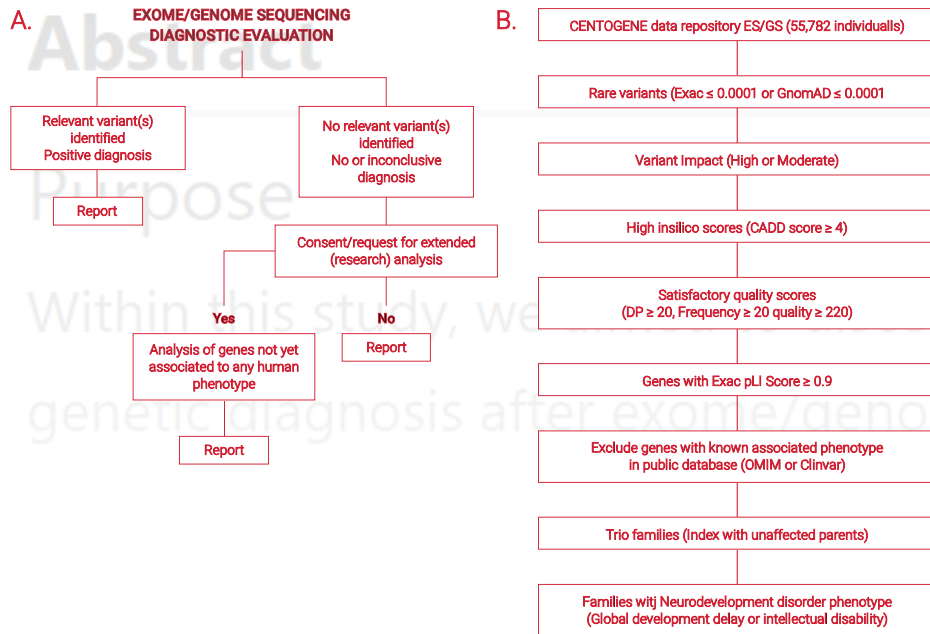
# 12

Scientific Impact: 12 novel candidate genes in 66 cases with no genetic diagnosis

# Leveraging Bio/Databank to unlock new disease insights

Driving innovation and insights with research

“Combining exome/genome sequencing with data repository analysis reveals novel gene-disease associations for a wide range of genetic disorders”



6

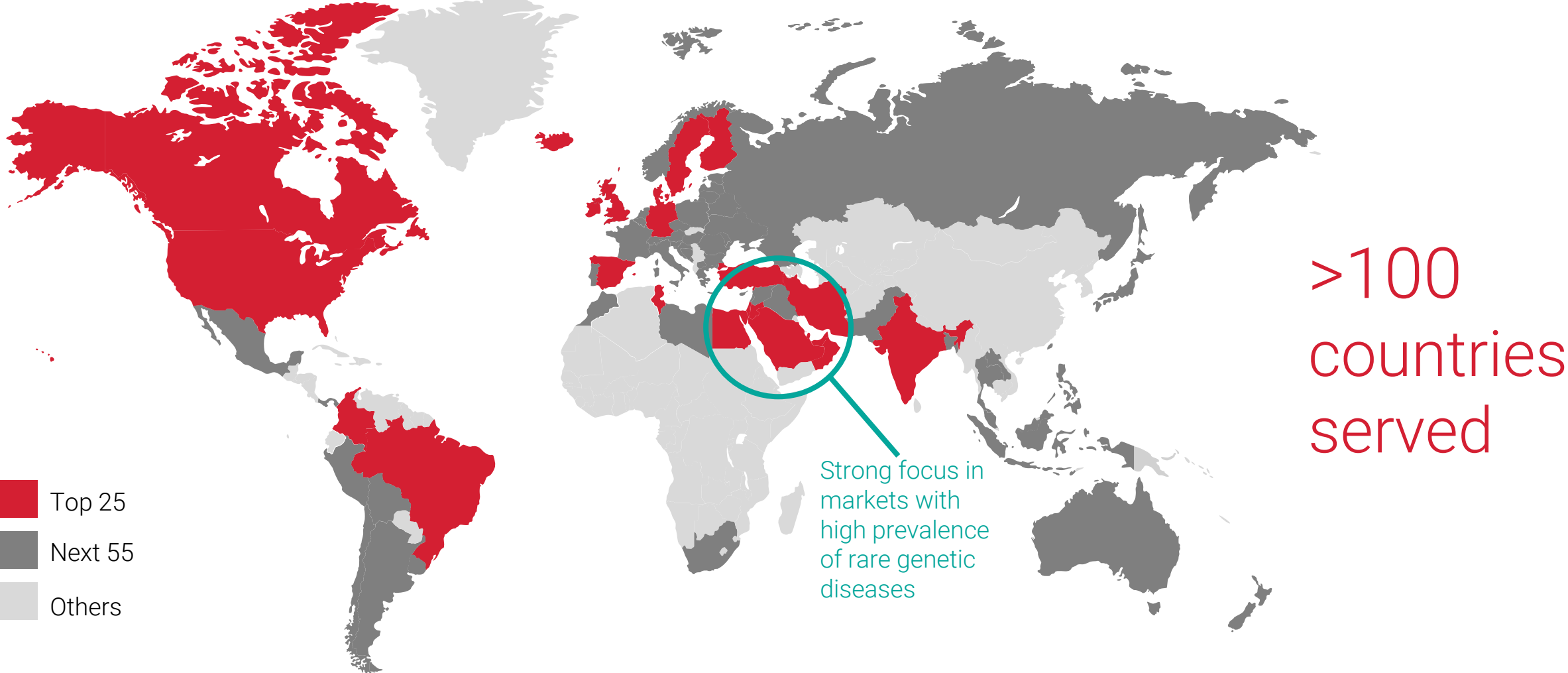
detected novel gene-disease associations based on ~40 patients from 13 countries

31

candidate genes which had little published evidence and no registered OMIM phenotype

# Global footprint in Clinical Diagnostics

Country ranking according to number of commercial orders received\*



\*Clinical Diagnostics commercial orders received 2012 to April 2021, order status "cancelled" excluded - Map for illustration purposes only

Clinical Diagnostics addressable market



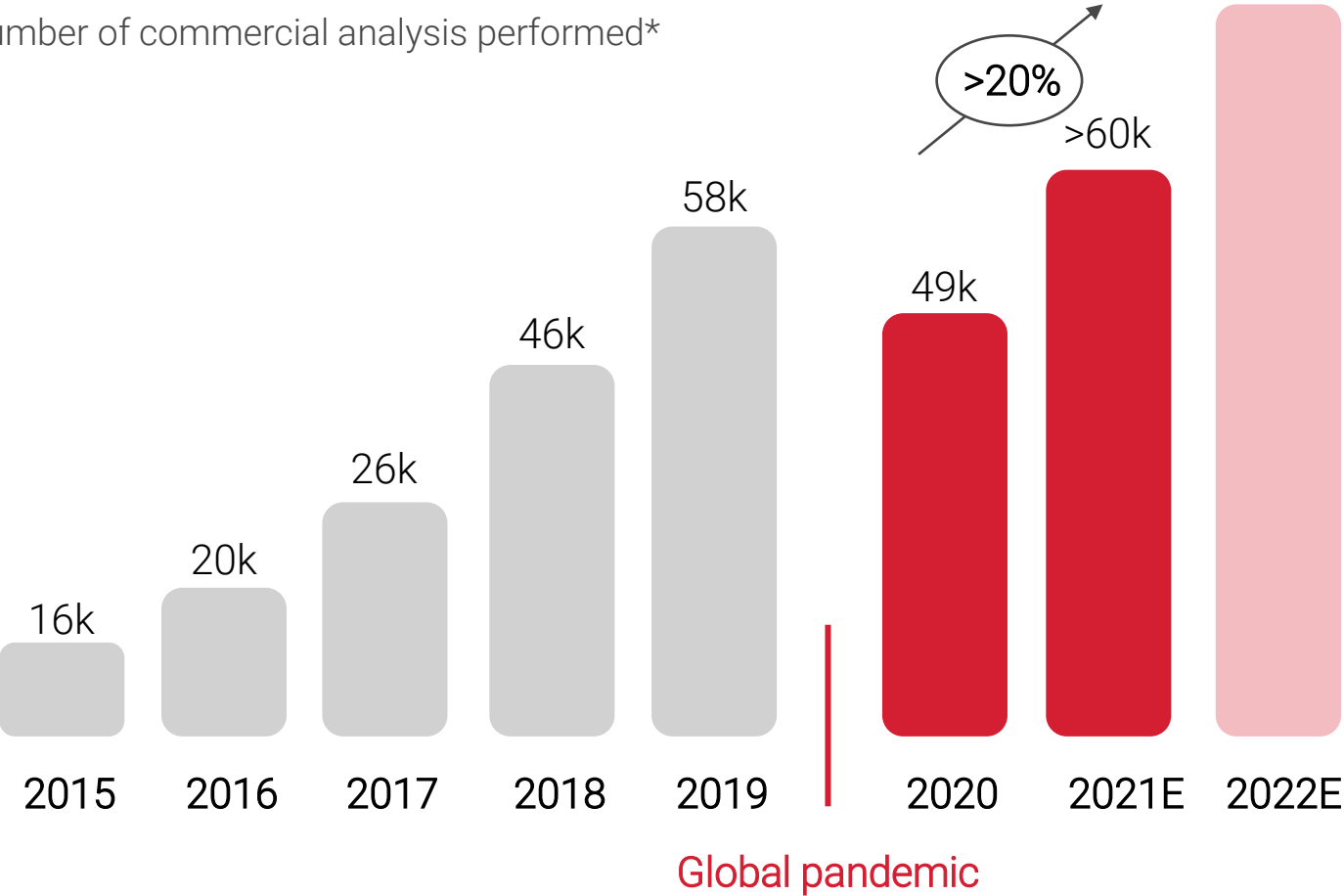
with CAGR of  
**~10%**

Source: Internal CENTOGENE 2020 estimates; 2018-2021 CAGR based on CENTOGENE market model

# Clinical Diagnostics growth

Return to pre-pandemic double digit growth in Clinical Diagnostics expected in 2021

Number of commercial analysis performed\*



Goal:  
Outperforming  
the market

\*Commercial samples only - excl. COVID-19 business, rounded

## Best-in-class insights based on superior technology

New CentoXome<sup>®</sup> with improved design and insights based on CENTOGENE's unique rare disease-centric Bio/Databank launched June 2021



Up to 20%  
Increased  
Diagnostic Yield

# NEW CentoXome<sup>®</sup>

~20,000 genes

≥ 98.0% ≥ 20x

~8,000  
clinical genes

≥ 99.5% ≥ 20x

OMIM<sup>®</sup>

HGMD<sup>®</sup>

CENTOGENE

Non-coding  
pathogenic variants

HGMD<sup>®</sup>

ClinVar

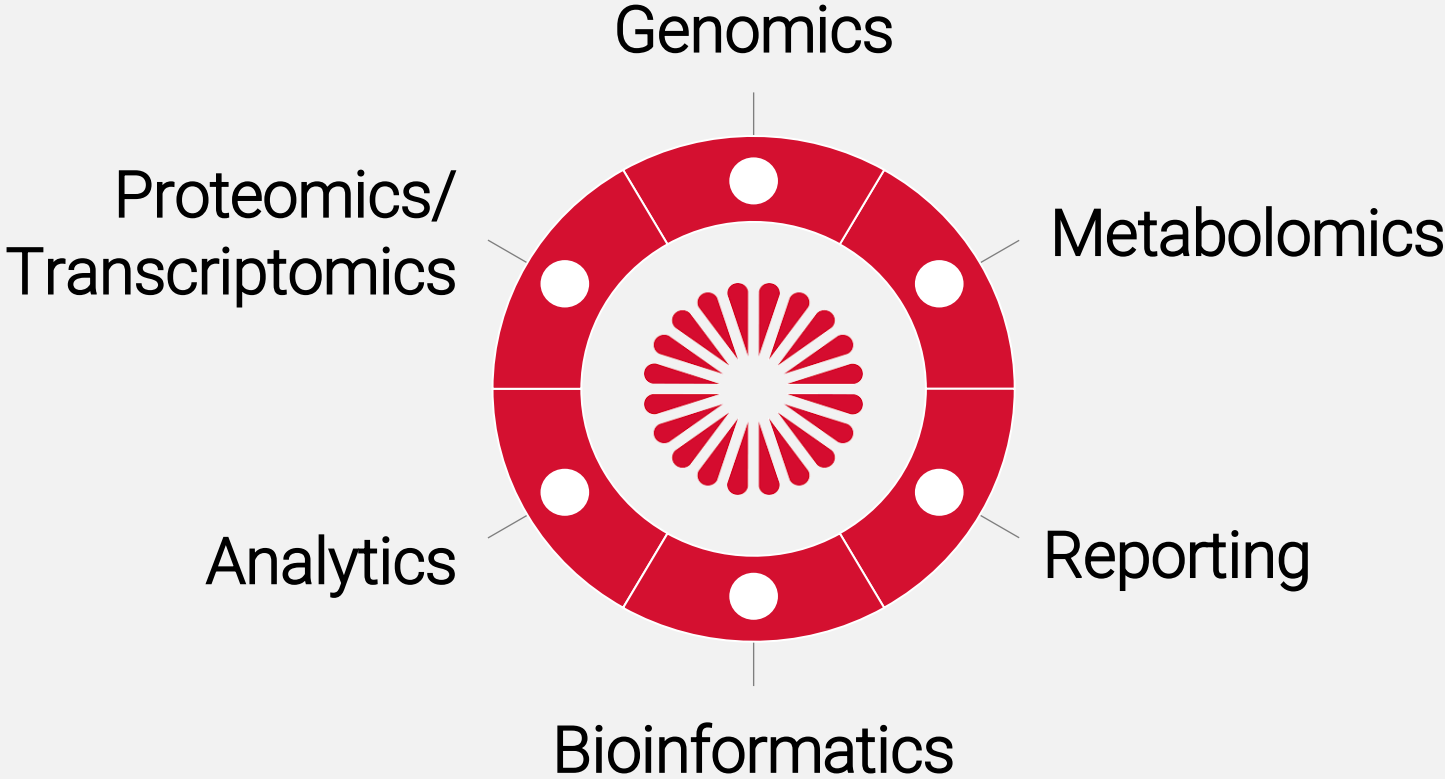
CENTOGENE

Mitochondrial  
genome

37 genes

# Innovation to sustain our leadership position in Clinical Diagnostics

CENTOGENE is continuing to innovate in Clinical Diagnostics based on its unique capabilities and expertise



## CentoCloud®

The icon shows a white computer monitor with a cloud inside and an upward-pointing arrow, symbolizing cloud storage or data upload.

## CentoMetabolome & Multiomics

The icon is a white chemical structure consisting of several interconnected rings and lines, representing a complex molecule or metabolite.





# 4. Enabling Differentiated Orphan Drug Development

# CENTOGENE's core business model for pharma

Data is THE key to creating solutions in rare diseases

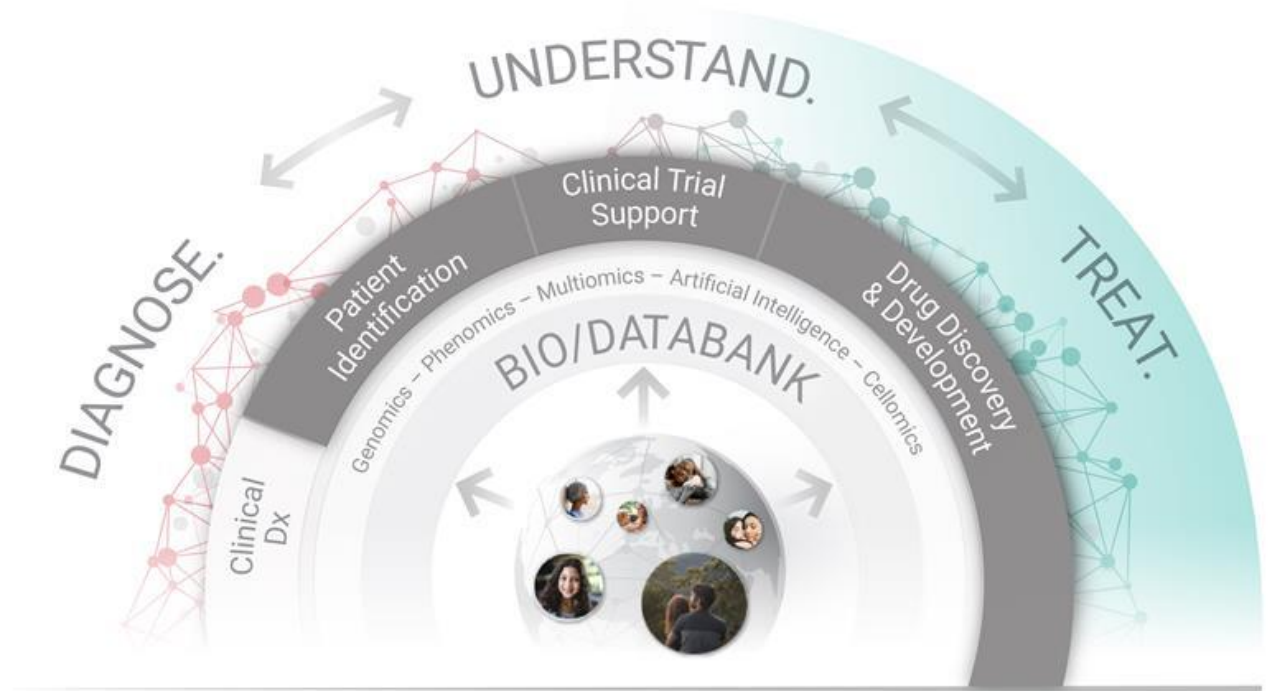
## Differentiation

Unique understanding of the molecular characteristics of rare diseases

Accumulation of **real-world patient data** in the CENTOGENE Bio/Databank

Ability to **correlate molecular characteristics** and patient genotypes with the respective **phenotypes**

Discovery of **differentiated treatments** for patients with rare diseases in **collaboration** with pharma



# CENTOGENE's unique value proposition to pharma

Turn data-centric insights into tangible assets and value for pharma



## Insight's Commercialization

Commercialization

Clinical Development

### Patient Identification

- Enable patient finding for the right treatment

### Clinical Trial Support

- Enable and accelerate recruitment
- Biomarkers as clinical endpoints
- Patient stratification

*Fueling the Bio/Databank*

\$

\$\$

\$\$\$\$\$



## Disease Offering

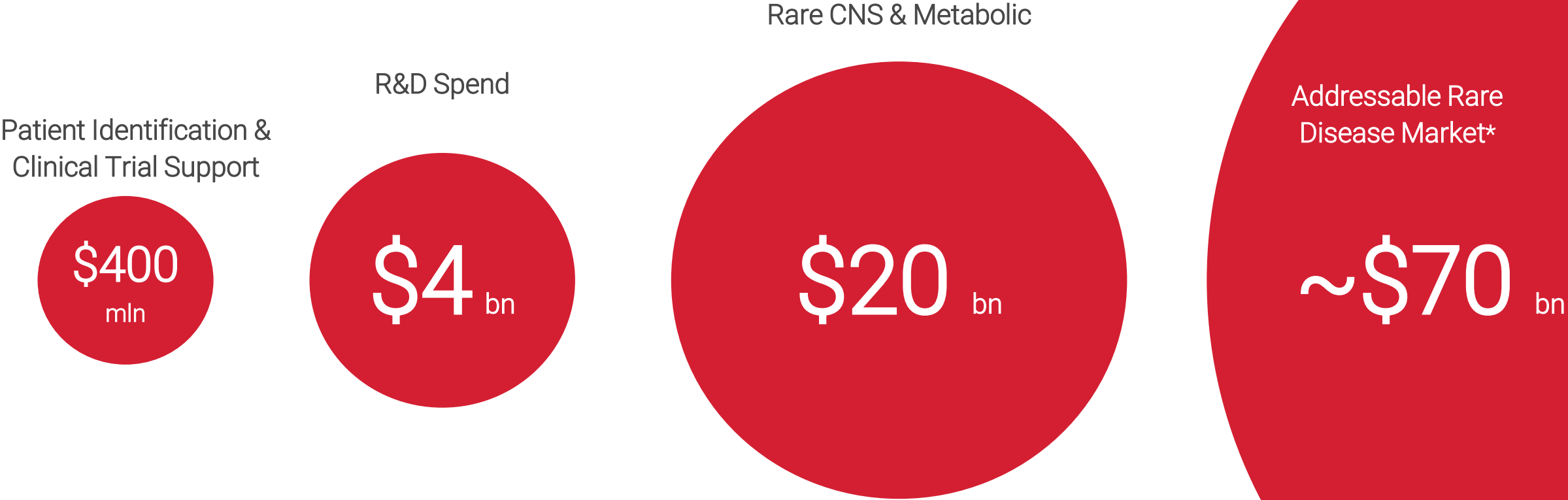
Research

### Drug Discovery and Development

- Biomarker IP
- Composition of matter IP
- Differentiated treatments

# Capturing increasing value in fast growing multi-billion rare disease market

Rare disease therapeutics CAGR +11% propelled by Orphan Drug Act



Above represents Centogene internal estimates based on total orphan drug market of \$156bn in 2021 by Evaluate Pharma® February 2020  
\* Addressable non-oncology rare disease market; Company estimate.

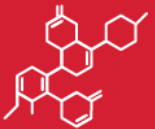
# Pharma is already buying into our concept of enabling precision medicine

Generate data and insight exemplified in our recent deals

## Our unique position ...



Understand the molecular characteristics of Parkinson's disease



Identify patients with frontal temporal dementia mutations



Turning these insights into precision medicine

## ... led to pharma engagements



ROPAD\* Study to genotype up to 12,500 patients with Parkinson's disease globally



EFRONT\* Study to determine prevalence of *GRN* in >3,000 frontotemporal dementia patients across Europe



Combining external hit discovery with CENTOGENE's novel disease insights to produce IND enabling therapies

# Uniquely positioned to further leverage patient identification and stratification with biomarker pipeline

Biomarker pipeline for future value generation

## Biomarker

Lyso Gb-1

Lyso Gb-3

Lyso 509

Lyso 459

30MD

Undisclosed

## Pathology

Gaucher

Fabry

NPC

NP A, B, C

AADC

MPSII

FRDA

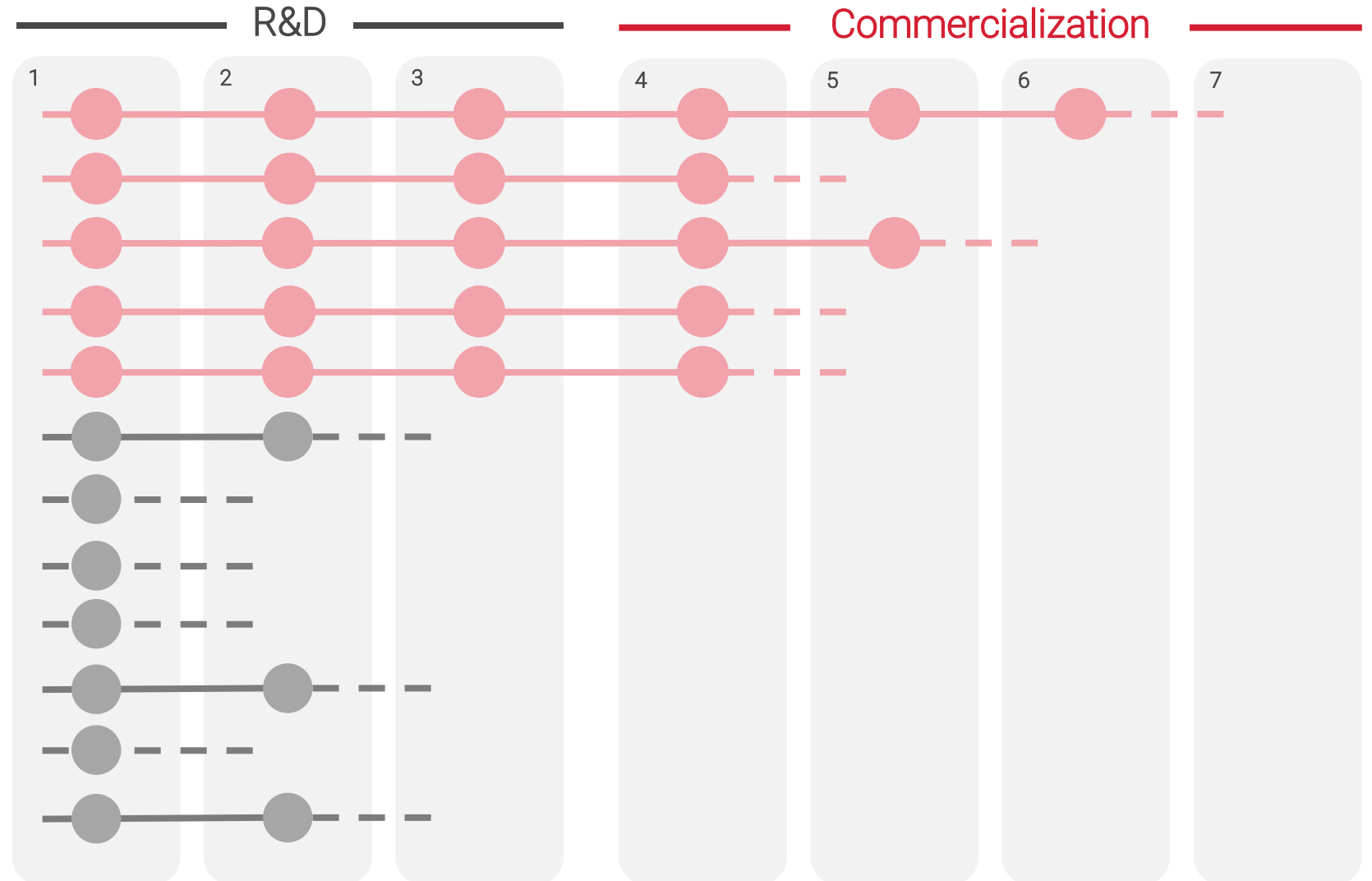
DMD

HAE

hATTR

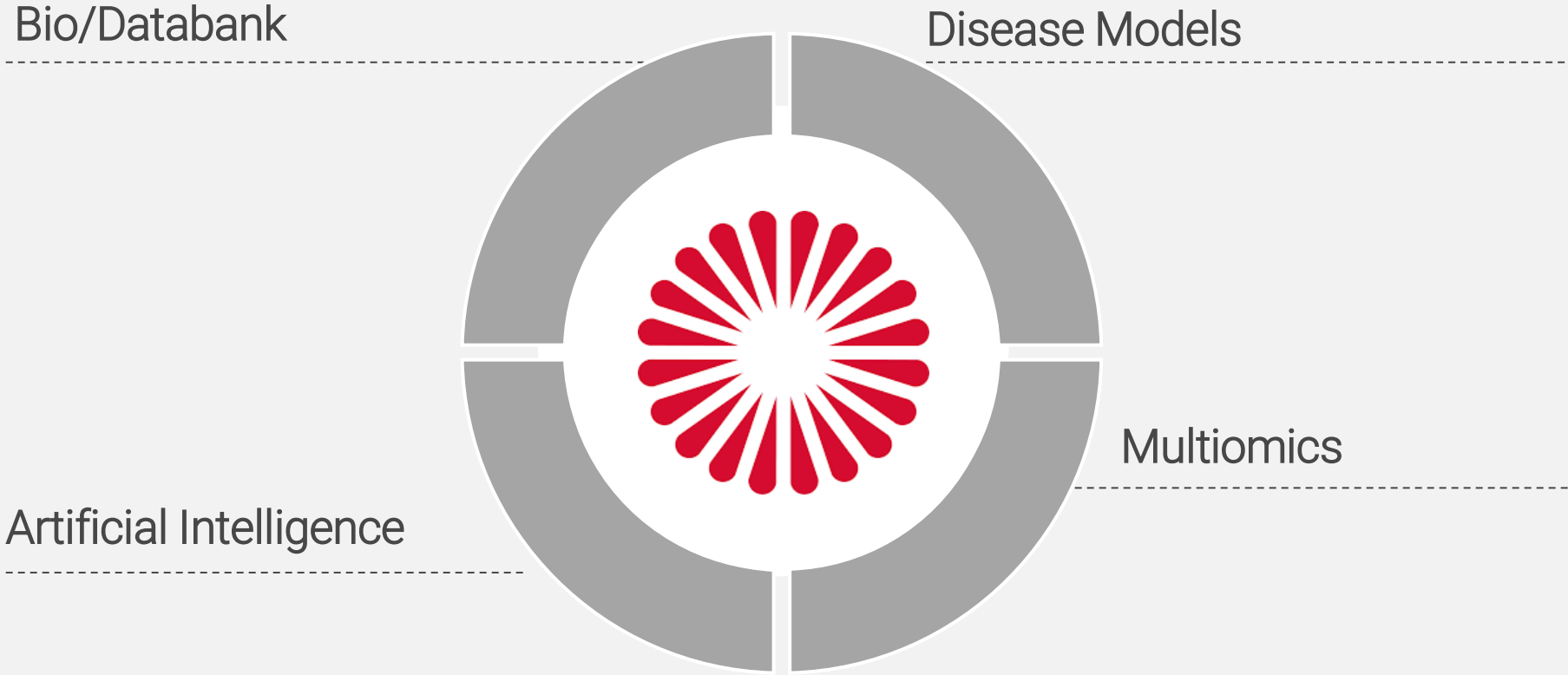
Parkinson's

Pompe



# Integration of data, AI, and multiomics leads to a new disease offering for Pharma

Enable differentiated drug discovery and development

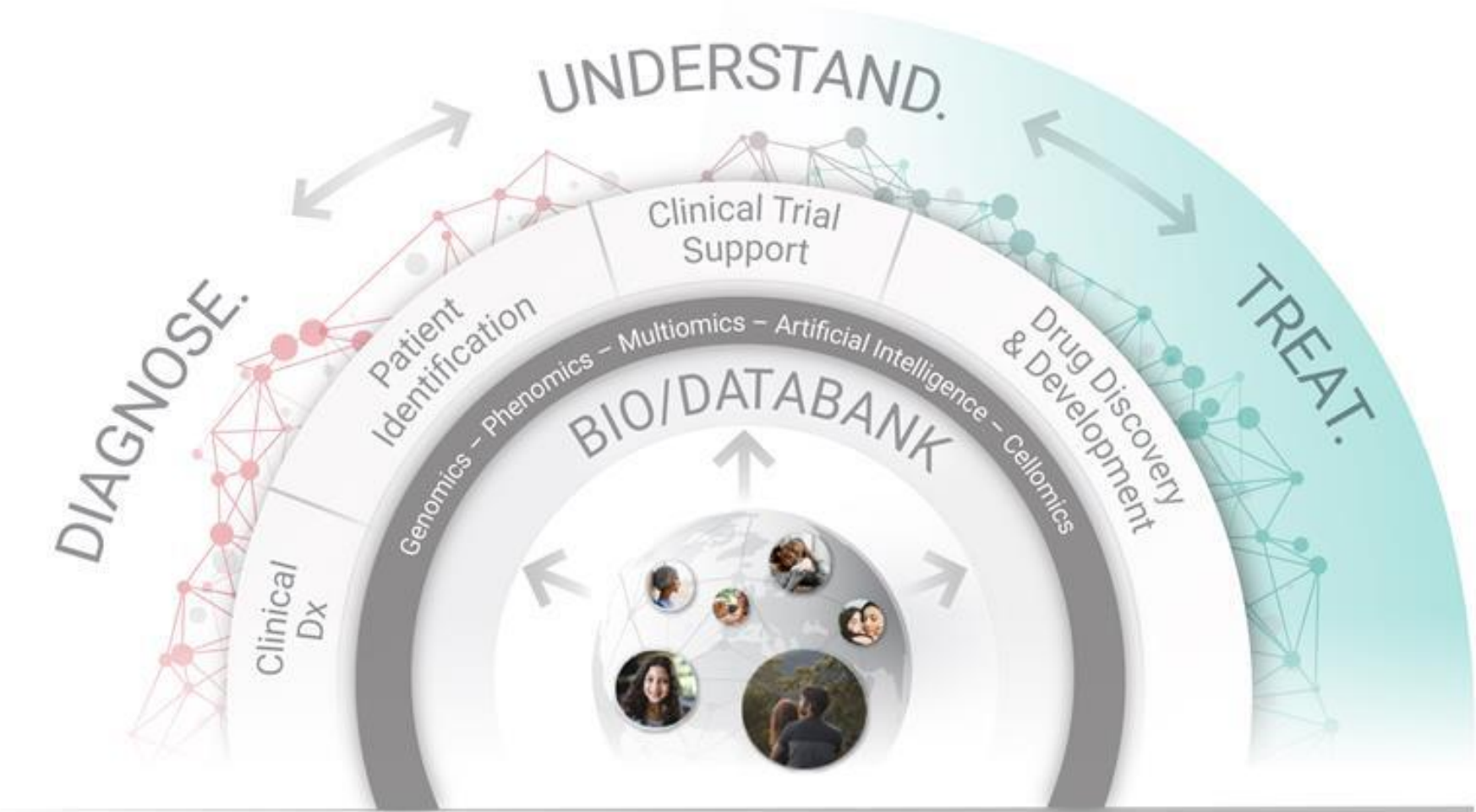


*Integrating key assets and capabilities allows the path of translational precision medicine for rare diseases to be addressed.*

# 5. Data-Driven Insights With Multiomics



# CENTOGENE business model and strategic value creation



# Genomics is important, but often not sufficient for a precise diagnosis

Biomarkers support the genetic diagnosis in complex or unclear cases

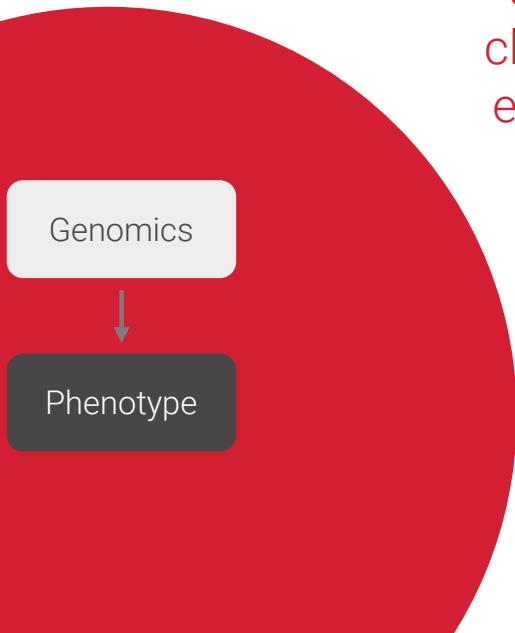
## Genomic Diagnosis



Two patients have the same genetic mutation leading to the same diagnosis.



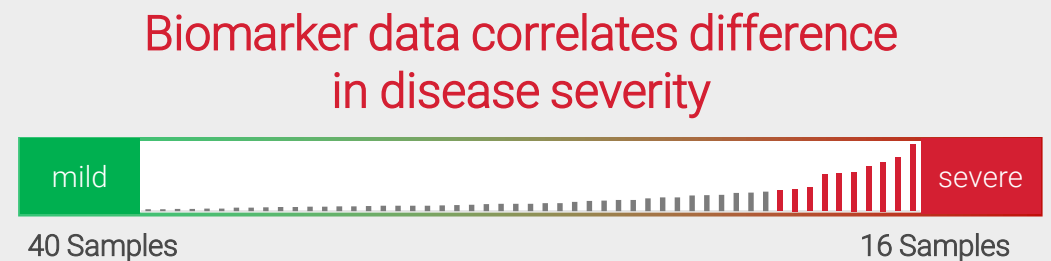
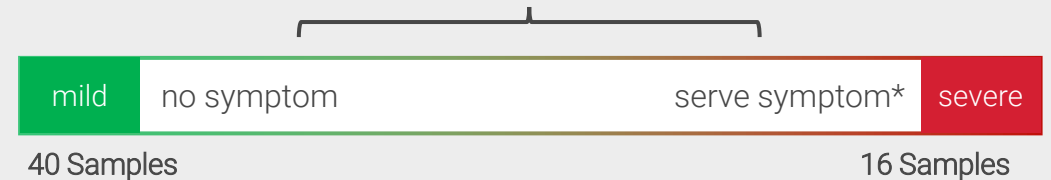
Same disease, but different clinical picture: one manifests early, and the other does not.



## Potential Schemes and Criteria for Stratification

**56x** the same genetic mutation but different disease severity

Homozygous variant for GBA p.N409S



Up to **25%** higher diagnostic yield for Gaucher/ Parkinson's cases compared to genomic data only

\*osteolytic lesions, osteonecrosis, pathologic fracture, bone crisis, hepatosplenomegaly, thrombocytopenia

# Genomics is important, but often not sufficient for a precise diagnosis

Biomarkers support the genetic diagnosis in complex or unclear cases

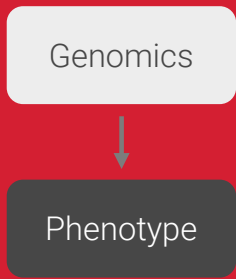
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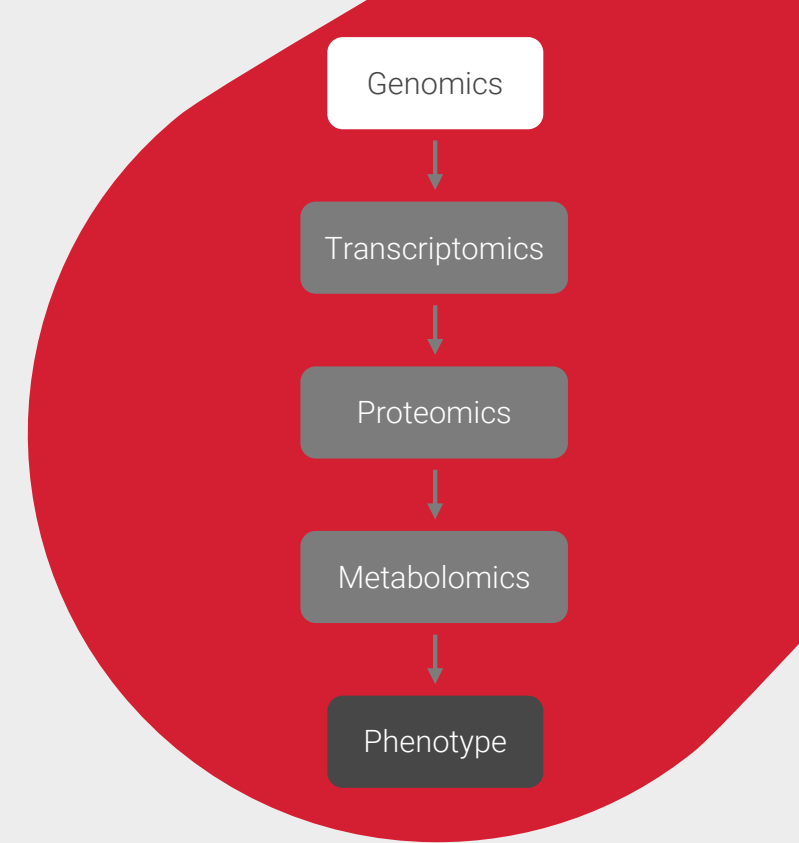


## Multimic Diagnosis



Two patients have the same genetic mutation, but different disease development

Multimic analytical insights lead to better disease models and thus to more precise medicine



# How we achieve this advantage

Multimic analysis approach to help end the diagnostic odyssey of patients with rare genetic diseases

## Metabolites – The Ultimate Readout

### Closest

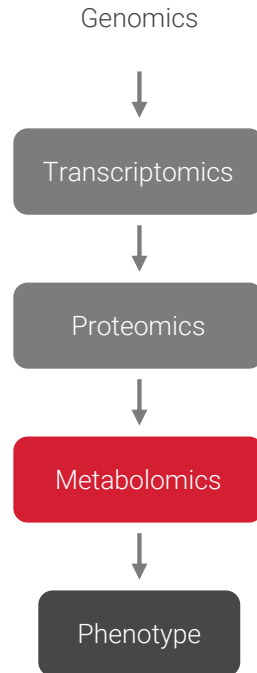
Metabolites are downstream products of the genome and a proxy to the functional phenotype of the cell

### Unique

Alterations of metabolites can be observed even when alterations of proteins and transcripts are not detectable.

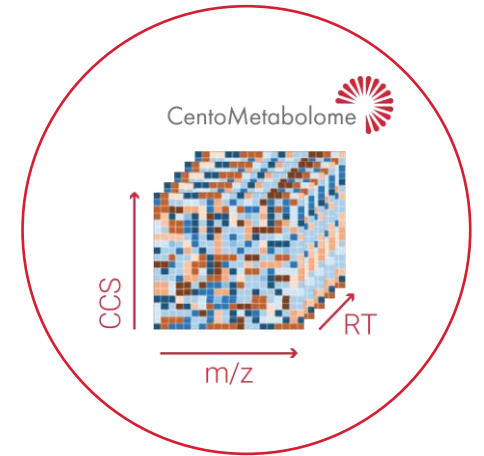
### Dynamic

Metabolites are quantitatively measured – not black or white as a variant – and mirror the dynamic development of the disease as well as different manifestations.



## CentoMetabolome

enables efficient identification of differences (single molecules and complex signatures) between metabolomic profiles of patient and control cohorts.



## Value of Biomarkers

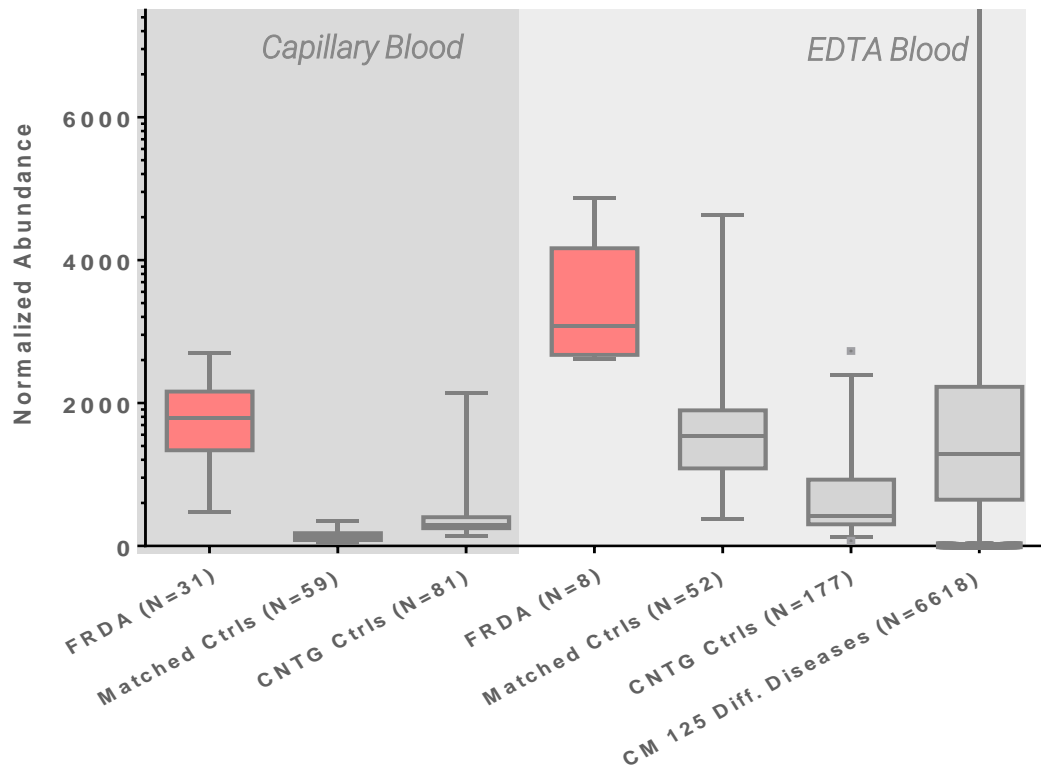
- Biomarker for diagnostics: -90% costs in the lab and higher diagnostic yield (e.g., +10%/+25% increased yield for complex Parkinson's/ Gaucher cases)
- Patient identification / diagnosis
- Clinical trial support
- Drug discovery and development

# New value creation with the CentoMetabolome platform

CentoMetabolome drives further value adding use cases on metabolomic data

## FRIEDREICH-ATAXIA

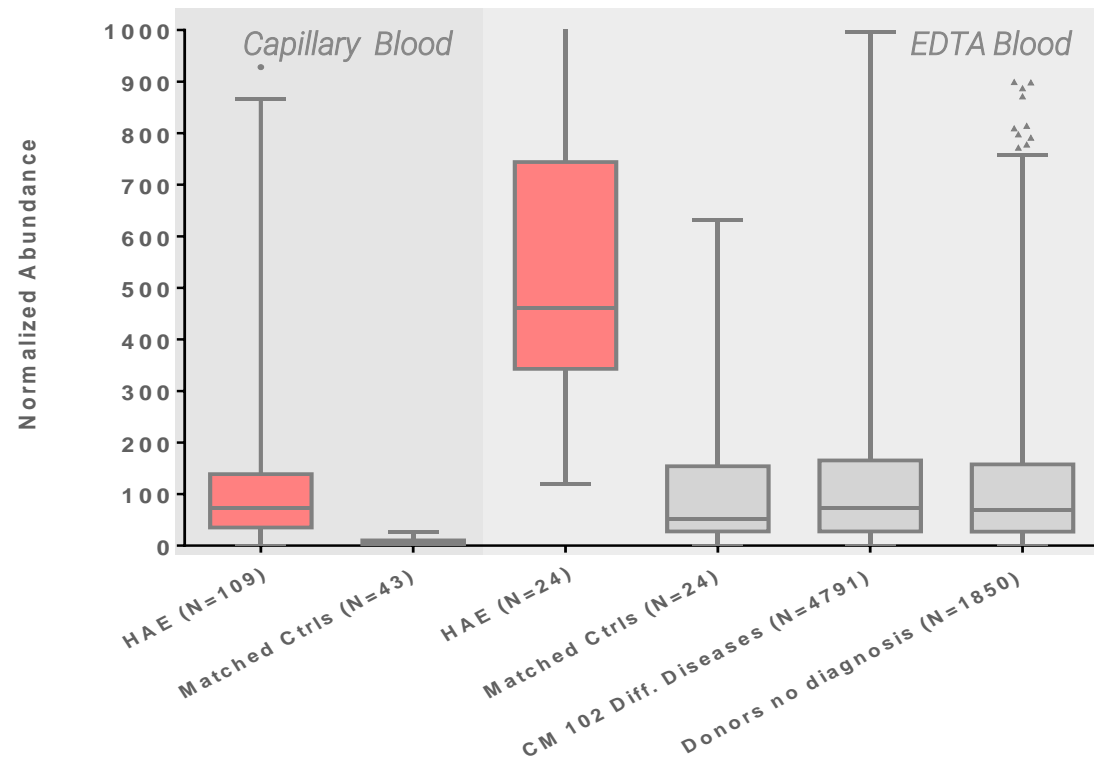
Identification of 11 potential biomarkers, which passed all quality filters and were confirmed with TQMS



## HEREDITARY ANGIOEDEMA

Ongoing analysis:

Two biomarker candidates passed first confirmation steps; several others in evaluation inclusive attack biomarkers



# Artificial Intelligence as an enabling link along the value chain

AI tools allow us to unlock multiomic data

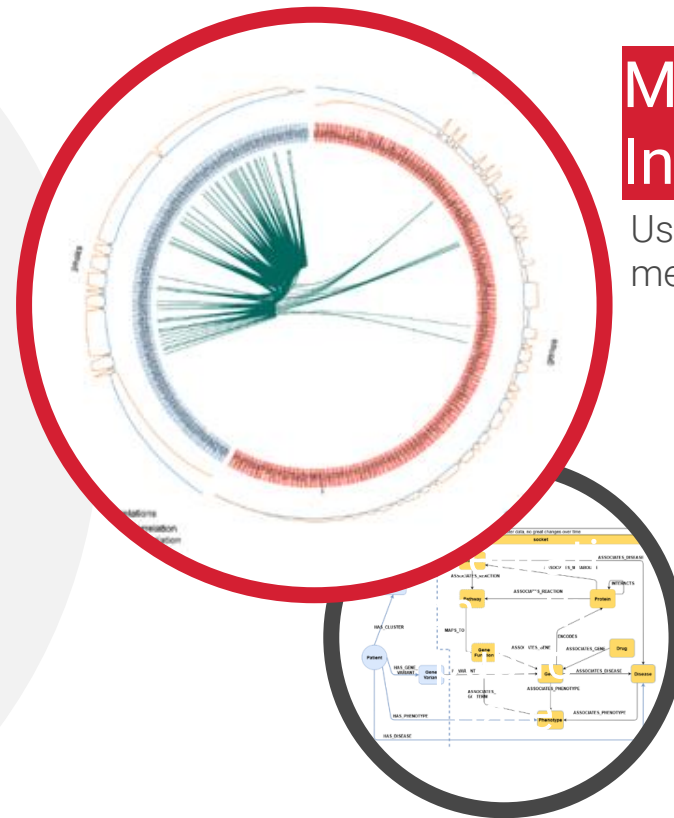
## Use the potential of AI...

**Discovery** of patterns and interdependencies in high-dimensional multiomic data

**Integration** of CENTOGENE's patient-based data with public data

**Analysis** of patient-based data through visualization in disease context

...to identify new genes, genetic modifiers, and pre-targets



## Multiomic Interdependencies

Use mutations and measurable effects on the metabolome to identify new pathways

## Integration With Public Data

Enable complex insights that take complete biological knowledge on genes, metabolites, and interactions into account.

## Visualization

Enable medical experts to better understand disease pathways of specific cohorts

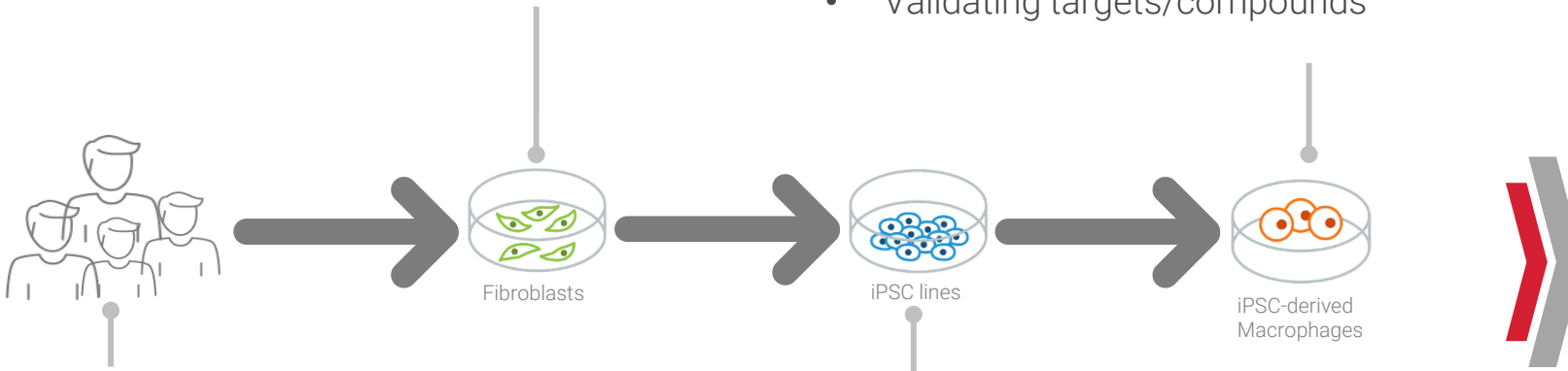
Integrated workbench for scientific multiomic workflows

# What can we do with a multiomic diagnosis?

Profiles gathered in Biobanks represented in cell-based model (e.g., Gaucher)

## Bio/Databank

- 80 Gaucher patients derived fibroblasts
- >80 Gaucher carriers derived fibroblasts



## Predictive Disease Model (cell-based model)

- Patient-derived macrophages
- Mimicking closely patient pathophysiology
- Generating omics data for new target discovery
- Validating targets/compounds

## CENTOGENE Bio/Databank

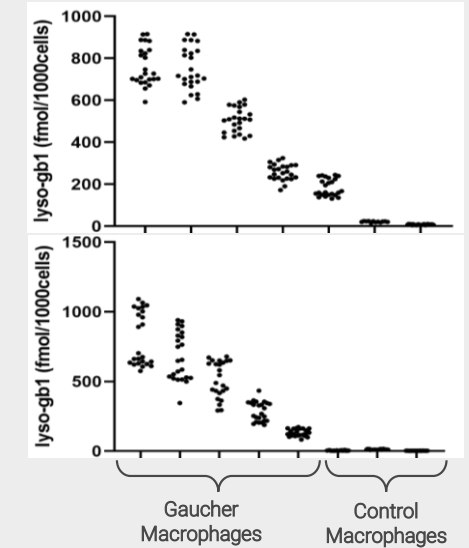
- Large patient cohorts
- Large data sets
  - Genetically defined patient
  - Specific Biomarker
  - Metabolomics data
- Diagnostic biomarker

## iPSC Bio/Databank

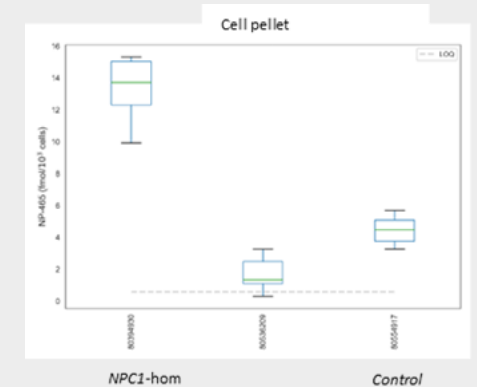
- >15 Gaucher patients IPSC lines
- Extensively quality controlled

We have done this for two diseases, Gaucher and NPC

## Severity Measure for Gaucher



## Severity Measure for NPC



# What is the potential?

iPSC technology as a tool for drug development in rare diseases

## Selection From Bio/Databank

- Patients derived fibroblasts
- Carriers derived fibroblasts

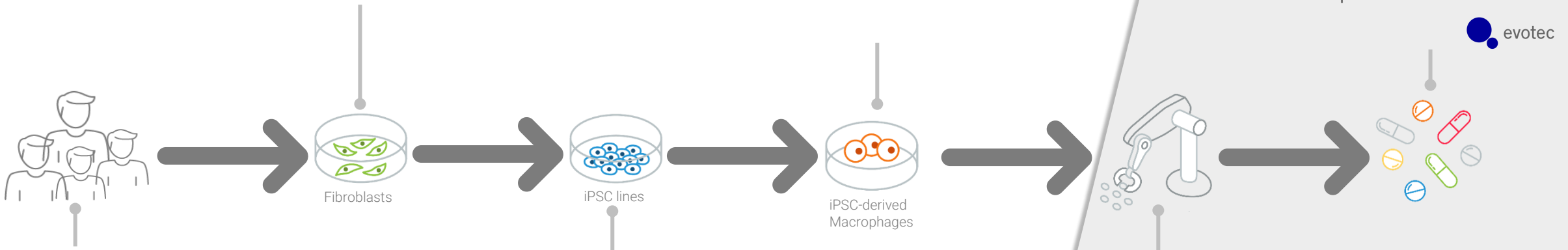
## Predictive Disease Model (cell-based model)

- Patient-derived macrophages
- Mimicking closely patient pathophysiology reducing
- Generating omics data for new target discovery
- Validating targets/compounds

**Potential:  
Develop Drugs for  
Diseases**

## Lead Optimization

- Extensive optimization/  
profiling from hit to lead  
compound with




## CENTOGENE Bio/Databank

- Large patient cohorts
- Large data sets
  - Genetically defined patient
  - Specific Biomarker
  - Metabolomics data

## iPSC Bio/Databank

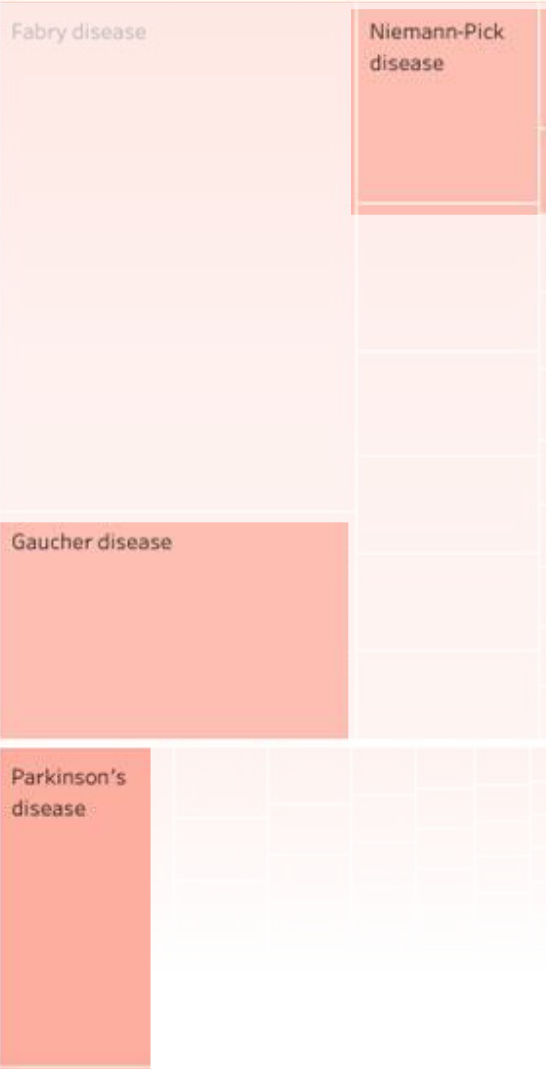
- Patients iPSC lines
- Extensively quality controlled

## Drug Screening and Validation


- Screening 250K compounds with 
- Validating top hits in patient derived macrophages




# Current focus diseases for full disease models



## Metabolic




Gaucher Disease

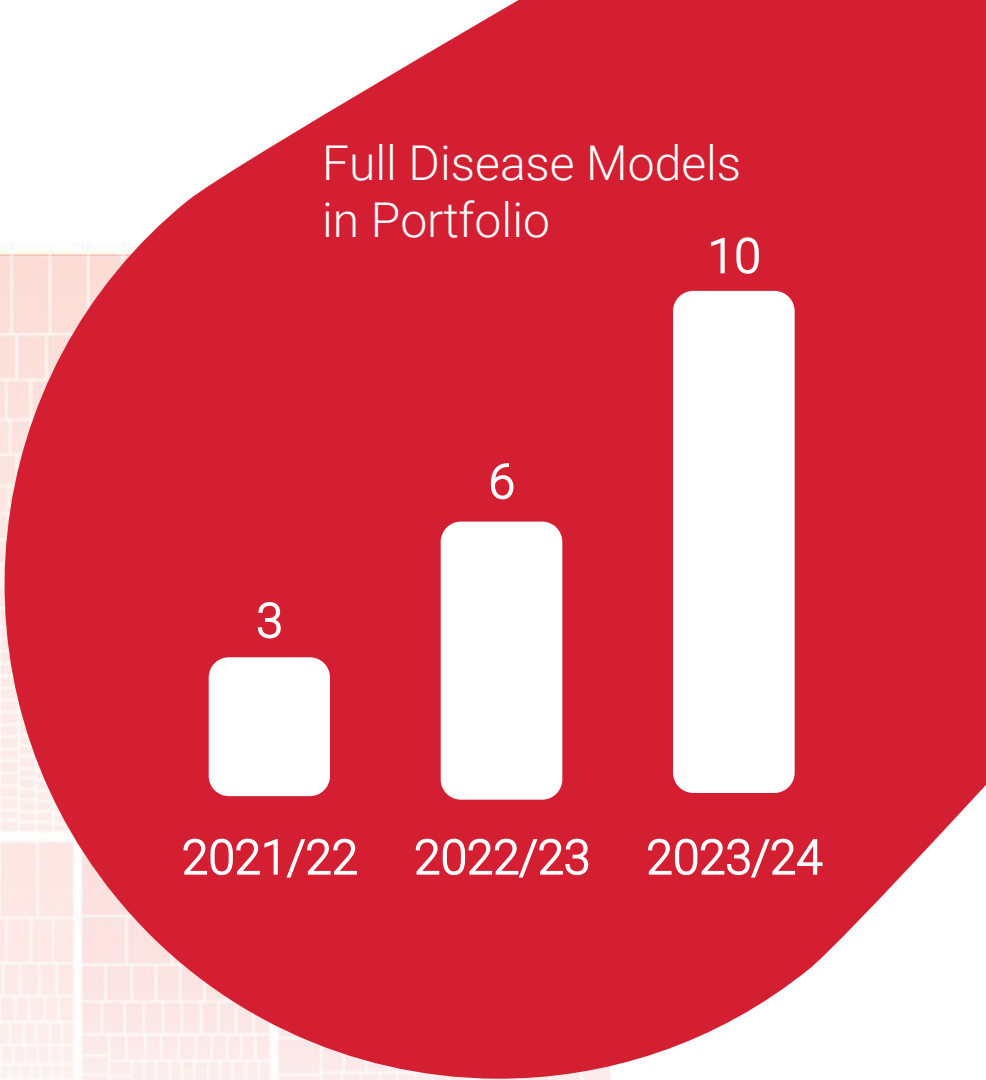


Niemann-Pick Type C - Disease

## Neurological



Parkinson's Disease





# 6. Finance Priorities and Process Optimization

## Introducing the new CFO

*René Just*

Let me  
introduce  
myself.



### Purpose

Unique focus on rare diseases

### Properties

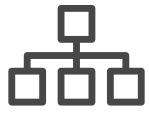
Growing Bio/Databank

### Potential

in bringing precision medicine to rare diseases

# Together we will drive results

Our priorities



## Organization

Supporting the organization in realizing the strategic plan



## Processes

Improving the reporting and closing cycles



## Transparency

Creating greater transparency



## Capital

Deploy capital efficiently with focus on core business



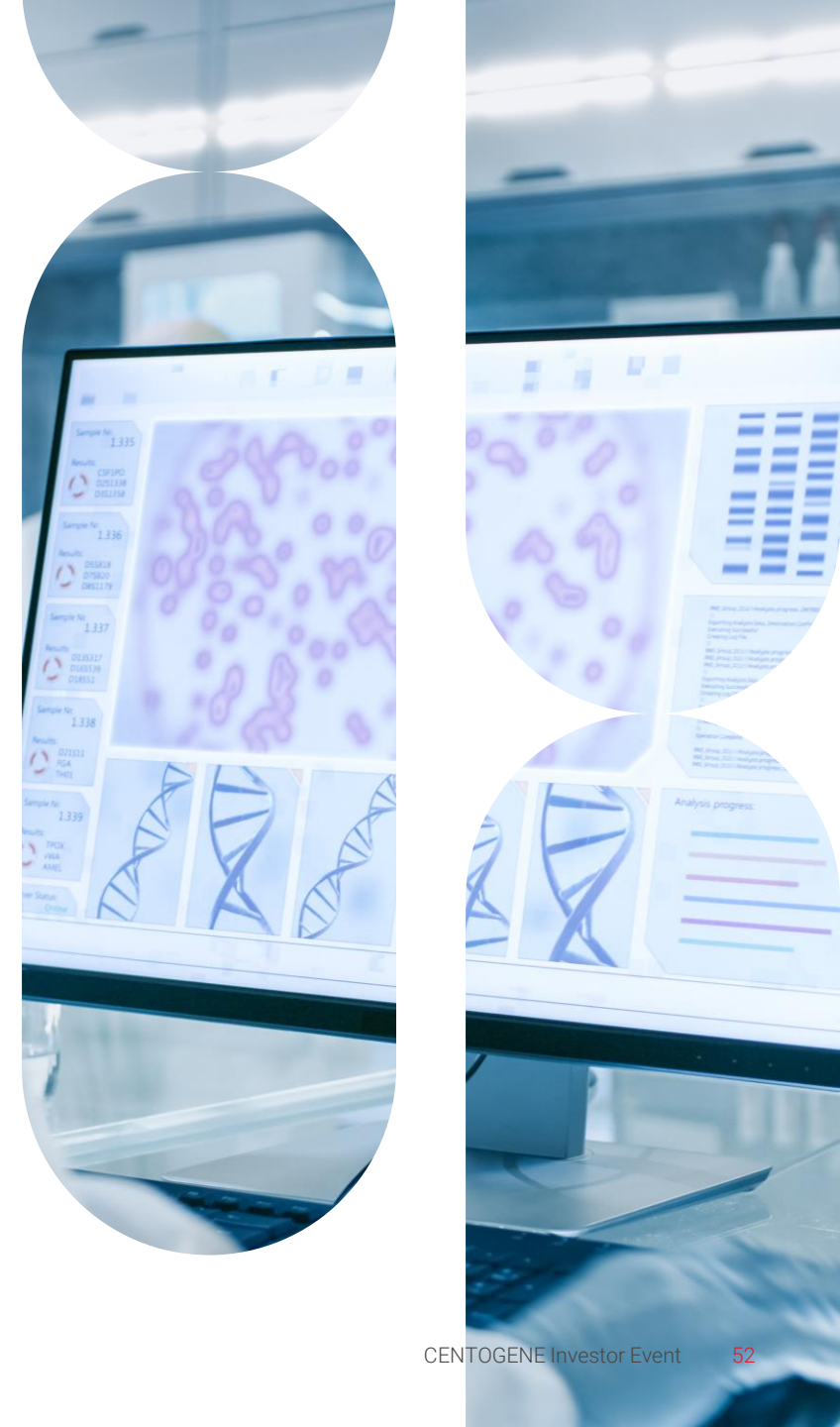
## Growth

Supporting the growth plan



## Values

Help articulating and setting organizational values



# Recent momentum indicates recovery of core business

Maintaining and building leadership in rare disease diagnostics

## Pharma

Contracts signed in 2021



Extension signed in Q1



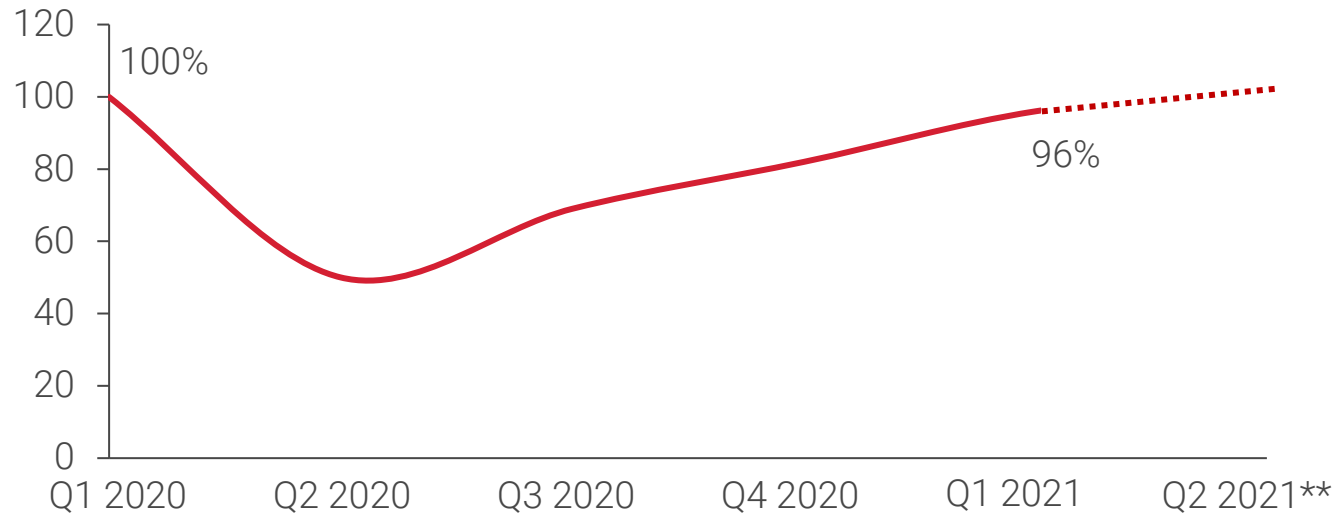
Extension signed in Q1



New contract signed in Q2

## Diagnostics

Sample Order Intake value in percent\*



\* Reflects quarterly average of value of weekly sample order intakes for diagnostic analysis in the Clinical Diagnostics segment relative to Q1 2020. The value for Q1 2021 is based on the first 12 weeks of the year 2021.

\*\* The value for Q2 2021 reflects calendar weeks 13 to 21.

## Recovery in Core Business

Dx revenue Q1 2021 above Q4 2020

Average weekly sample order intake value in Q2 2021 above same period prior year \*\*

Extension of Takeda and Denali collaboration

New Alector contract regarding frontotemporal dementia

>25,000 patients added to rare diseases-centric Bio/Databank



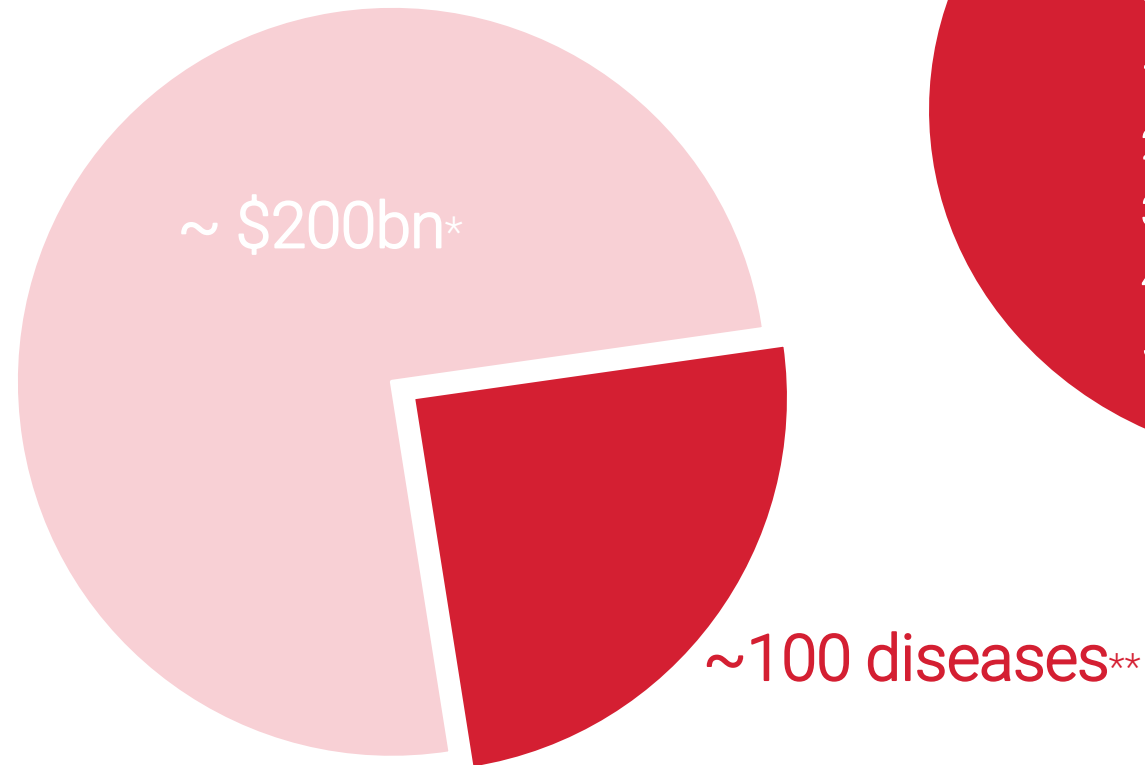
# Summary

# Tremendous future value potential for CENTOGENE by enabling orphan drug development

Future potential of capturing share of orphan disease market

## CEN TOGENE Key levers

- > Superior patient diagnostic insights
- > Accelerate clinical trials
- > De-risk clinical trials
- > Increase chance of approval
- > Maximize re-imbursement



Total estimated addressable future rare disease market  
2031\*

## Estimated annual royalty revenue potential \*\*\*

- 1% ≈ \$ 0.5 billion
- 2% ≈ \$ 1.0 billion
- 3% ≈ \$ 1.5 billion
- 4% ≈ \$ 2.0 billion
- 5% ..

\*Above represents CENTOGENE's internal estimates based on the total orphan drug market of \$156bn in 2021 by Evaluate Pharma® February 2020, estimating the addressable non-oncology rare disease market at ~\$70bn in 2021 and applying the CAGR of 11% for 10 years, leading to an estimated future rare disease market potential of ~\$200bn in 2031.

\*\*Future market potential estimate based on peak sales of \$500M per orphan drug for 100 diseases.

\*\*\* Estimated annual revenue potential from potential future royalty share calculated on the basis of the estimated future rare disease market potential 2031.

## Investment summary

Empowering new management team to execute on mission

Clear focus on core rare disease business

Return to pre-pandemic sales growth trajectory in core business segments

**Goal of enabling cure of 100 rare diseases in 10 years**

## Tracking Our Mid-Term Progress

- Revenue in Dx and Pharma segment to outgrow the market
- Reach 1 million patients in Bio/Databank
- Grow physician network of active users
- Reach 10 full disease models
- Sign 2-4 strategic partnership deals towards enabling therapy development





THANK YOU FOR YOUR  
ATTENTION.

Q&A