Transforming Global Genetic Data into Medical Decisions
CENTOGENE is dedicated to transforming the science of genetic information into solutions and hope for patients with rare diseases and their families.

We achieve this by:

› Leveraging the world’s largest database in rare genetic disorders with genetic, proteomic, metabolomic, and clinical information – CentoMD®

› Applying our knowledge derived from our global diagnostic testing services – addressing the worldwide heterogeneity in ethnicities

› Guaranteeing the highest quality in our processes based on the highest level of accreditation
What Drives CENTOGENE

Our goal: providing precise medical diagnosis of inherited diseases at the earliest possible moment; transforming medical expertise and analytical information into actionable results for physicians, patients, and pharmaceutical partners.

Our commitment: Life-long commitment to all rare disease patients - driven by our passion and continuous advancements in providing world-class genetic testing and transformative medical solutions.

Our work does not end by just delivering a medical diagnosis. Over 60 medical experts, human geneticists, and researchers work together with clinical, medical, and scientific partners worldwide. Strategic pharmaceutical alliances in the orphan drug sector
Creating solutions for pharmaceutical companies that help accelerate the development of orphan drugs: patient identification and screening, biomarker

Rapid medical diagnosis of rare hereditary diseases through the broadest genetic testing portfolio, and building the global knowledge base of rare disease patient populations
Proven by Numbers

**Have a look behind the scenes.** Not all company value can be seen at first sight. Convincing numbers that underline CENTOGENE’s leading position as a global biotech company are found everywhere.

<table>
<thead>
<tr>
<th><strong>7</strong></th>
<th><strong>13</strong></th>
<th><strong>&gt; 50</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Global affiliations</td>
<td>Technological platforms</td>
<td>Nationalities of our employees</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>&gt; 120</strong></th>
<th><strong>450</strong></th>
<th><strong>&gt; 7,500</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Countries</td>
<td>Employees</td>
<td>Confirmed cases of Fabry Disease</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>&gt; 150,500</strong></th>
<th><strong>12.2</strong></th>
<th><strong>3.1</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Samples received Jan - Dec 2019</td>
<td>Million unique variants in CentoMD®</td>
<td>Billion alleles identified in CentoMD®</td>
</tr>
</tbody>
</table>
The outcome of growth and expansion at CENTOGENE is the inauguration of new locations. As a cosmopolitan company, we have a strong international footprint.
Solid Growth in Just Over a Decade

**2006**
Diagnostics in neurogenetic diseases

**2006***
- Biomarkers
- MLPA
- qPCR
- Whole exome sequencing

**2016**
- CentoCard®
  The logistic solution
- >180 NGS panels
- Metabolomic platform
- Oncogenetic testing

**2016**
- Whole genome sequencing
- CentoMD®
  The mutation database
- Proteomic platform
- Microarrays
- High throughput genomic facility
- Non-invasive prenatal testing (CentoNIPT®)
- Transcriptomics

**2018**
- Carrier screening (CentoScreen®)
- > 9,000 different test assays

**2020+**
- Artificial Intelligence initiative
- Providing world-class genetic testing and life-changing solutions for all rare disease patients

**2019**
- iPSC program
- IPO
Achieving a Positive Change in our Patient’s Life
CENTOGENE charity testing program

At the forefront of all our activities, we are dedicated to offering the greatest medical benefit to every patient, regardless of their access to medical diagnosis.

Testing for rare hereditary diseases is becoming more important and is now considered a common diagnostic tool, with the arrival of better, more effective options for the treatment of certain diseases.

Most insurance providers cover genetic testing services, but each situation is unique. If a patient is uninsured or unable to cover the costs otherwise, CENTOGENE offers genetic and biochemical testing free of charge on a research basis through our CENTOGENE Charity Testing Program (CCTP).

As part of CCTP, we are able to bring not just hope to rare disease patients, but also life-changing impact.
CentoCard® is easy to handle: samples are stable once dry and can be mailed directly by regular post.

Samples collected on CentoCard® are not sensitive to temperature or time, nor are they considered biohazardous.

CentoCard® is suitable for any analysis and testing method, including whole exome and whole genome sequencing.

**Dried blood spot (DBS) filtercards for patient sample collection and shipment.** The simplest way to ship biological samples – as easy as mailing a postcard – making genetic testing accessible to anyone anywhere.

**CENTOCARD® IN DETAIL:**
Your solution for smarter diagnostic communication. CentoPortal® is a user-friendly, online, web-based ordering portal designed to assist you at every step of processing your patients’ samples.

CentoPortal® allows you to instantly create an account and place an order in a few easy steps. It is designed to save time and reduce overall workload such that you can:

› Order a test in a few easy steps
› Obtain an overview of your patients and analyses performed
› Track your samples
› Download your patients’ medical reports with the highest data protection and privacy standards
For many patients the combination of symptoms does not allow a clinician to pinpoint a specific diagnosis. Therefore, ordering genetic testing becomes complex and might involve a stepwise testing strategy, which often significantly increases costs and time to diagnosis. CentoXome®, our one-step whole exome sequencing (WES) test, solves complex clinical cases quickly and cost-effectively. By using CentoXome® as a first-tier test alongside the unique option of copy number variant (CNV) detection, the need for additional evaluations is decreased – bringing fast and affordable answers to rare disease patients and their families.

**KEY BENEFITS OF WHOLE EXOME SEQUENCING (WES) WITH CNV**

- A cost-effective, one-step solution by sequencing the entire protein coding region of an individual’s DNA comprised of ~20,000 genes (covering about 85% of all known disease-causing mutations)

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By choosing CentoGenome®, the most comprehensive whole genome sequencing (WGS) testing solution, healthcare professionals can diagnose their patients and end their diagnostic odyssey, saving valuable time on their road to treatment. Through its ability to cover the entire coding and non-coding regions of the genome, CentoGenome® helps with solving complex and undiagnosed cases, making it the ideal first-line genetic testing solution. Furthermore, even WES negative cases can benefit from WGS in 10-15% of the cases.

**KEY BENEFITS OF WHOLE GENOME SEQUENCING (WGS)**

- The first-line testing solution by reliably detecting virtually all disease-causing genetic variants (covering about 99% of the genome)
CentoXome® and CentoGenome®

Depending on the sample origin, genomic testing can lead to a diagnosis in 20 – 70% of patients suspected to suffer from rare genetic conditions.

**Highest quality for both tests**
Whether you chose CentoXome® or CentoGenome®, we guarantee superior technical, scientific, and medical expertise, reducing diagnostic uncertainties, and supporting patient diagnosis.

- Both tests deliver high diagnostic yields across a variety of molecular etiologies
- CentoGenome® can provide a diagnosis even in cases where WES did not

<table>
<thead>
<tr>
<th>Coverage</th>
<th>CentoGenome®</th>
<th>CentoXome®</th>
</tr>
</thead>
<tbody>
<tr>
<td>~99% of the genome covered at ≥10x</td>
<td>~98% of the targeted regions covered at ≥20x</td>
<td></td>
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</table>

<table>
<thead>
<tr>
<th>Gene regions</th>
<th>CentoGenome®</th>
<th>CentoXome®</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coding (exonic) and non-coding regions (intrinsic and regulatory regions, and splice sites)</td>
<td>Coding (exonic) regions and exon/intron boundaries</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Uniformity of sequencing data</th>
<th>CentoGenome®</th>
<th>CentoXome®</th>
</tr>
</thead>
<tbody>
<tr>
<td>Highest</td>
<td>High</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Types of pathogenic variants detected</th>
<th>CentoGenome®</th>
<th>CentoXome®</th>
</tr>
</thead>
<tbody>
<tr>
<td>SNVs, InDels, and CNVs*</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Large and more complex structural variants</td>
<td>Yes</td>
<td>Limited</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Clinical utility</th>
<th>CentoGenome®</th>
<th>CentoXome®</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diagnostic yield</td>
<td>Highest (reveals also variants not identified by WES)</td>
<td>High</td>
</tr>
<tr>
<td>Reduction of time-to-diagnosis</td>
<td>Highest (when done as first step)</td>
<td>On average lower than WGS</td>
</tr>
<tr>
<td>Value of data for potential future reanalysis</td>
<td>Highest</td>
<td>High</td>
</tr>
</tbody>
</table>

* SNVs: single nucleotide variants
InDels: small insertions and deletions
CNVs: copy number variants
The complete carrier screening panel for responsible family planning. Most people can be carriers of a disease-causing change without knowing it. CentoScreen® helps healthy, and especially consanguineous, couples understand if they are carriers of any of the more than 300 relevant recessive genetic diseases before pregnancy. With ≥99% coverage, it provides couples and physicians with the highest confidence in test results before pregnancy.

Why choose CentoScreen®?

1. Comprehensive carrier screening panel targeting the most relevant autosomal and X-linked recessive diseases
2. Sequencing of the coding regions +/-20 flanking intronic bases of 332 genes
3. Integrated copy number variation (CNV) reporting for 34 genes where high-frequency structural variants have been reported
4. Covers most relevant disease-causing variants as described in HGMD® and proprietary CentoMD® database, including deep intronic and regulatory mutations
Illumina VeriSeq™ NIPT Solution v2: Non-invasive prenatal testing that provides a safe and accurate screen for the most common prenatal chromosomal abnormalities. CentoNIPT® is performed on a single maternal blood sample and combines the latest NGS technology with the highest quality medical reporting. It provides unparalleled accuracy and detection compared to other noninvasive testing methods, such as ultrasonography, nuchal translucency testing, or maternal serum screening.

WHAT DOES CENTONIPT® SCREEN FOR?

› Down syndrome (Trisomy 21)
› Edwards syndrome (Trisomy 18)
› Patau syndrome (Trisomy 13)

THE TEST ALSO DETECTS ABNORMALITIES OF THE SEX CHROMOSOMES:

› Turner syndrome (Monosomy X)
› Klinefelter syndrome (XXY)
› Jacobs syndrome (XYY)
› Triple X syndrome (XXX)

WHY CHOOSE CENTONIPT®?

1. Maximum certainty - lowest test failure rate of all NIPT technologies
2. 100% safe for mother & child - only 9 ml of peripheral blood from the mother required
3. Fast & reliable results - within 5 business days of sample receipt
4. Test as early as possible - from the 10th gestational week on
Biomedical-Assay/Testing

CENTOGENE works alongside academic and pharmaceutical partners, as well as patient organizations to develop new diagnostic assays and biomarkers that improve the condition and monitoring of patients affected by hereditary diseases.

**Biological Validation**
- **Analytical validation**: High resolution hybrid mass spectrometry
- **Clinical validation**: Test validation in clinical set-up according to CAP/CLIA guidelines
- **Clinical application**: Diagnosis, prognosis and therapy monitoring

**Biomarkers for Therapy Monitoring and Evaluation**
Glucosylsphingosine (Lyso-Gb1) is a great example at CENTOGENE of an excellent biomarker used by our scientists for the accurate screening, diagnosis, and follow-up (monitoring) of Gaucher disease (Trait and state marker).

**Individual Lyso-Gb1 Levels:**
- 45u/kg
- 60u/kg
- 75u/kg

Arrow labelling events of bone crises, in the mean 6-8 weeks after increase of Lyso-Gb1

Time points of Lyso-Gb1 measurements
NEW PROTEOMICS ASSAY FOR DIAGNOSIS OF HEREDITARY ANGIOEDEMA:

› Hereditary angioedema (HAE) is a disorder that results in recurrent attacks of severe swelling
› Type I and II are caused by a mutation in the SERPING1 gene (C1 inhibitor protein)
› This new screening method is based on C4 and C1-INH protein quantification directly in dried blood spots using mass spectrometry
**CentoCancer**

**Our most complete oncogenetics panel for hereditary mutations.** CentoCancer® has now been extended to 72 genes, allowing you to choose the best possible medical management plan and treatment decisions for your patients and their families. Each gene in CentoCancer® has been carefully selected based on its risk potential in the development of one or more of the following cancers:

- Breast
- Ovarian
- Colorectal
- Gastric
- Thyroid
- Endometrial
- Pancreatic
- Melanoma
- Renal
- Prostate

**WHO SHOULD CONSIDER CENTOCANCER® FOR GENETIC TESTING?**

- Individuals with a positive personal history of early-onset cancer, rare cancer, bilateral cancer, or multiple primary cancers
- Unaffected individuals with a positive family history of recurrent cancer, rare cancers, or early-onset cancers
- Individuals in whom the suspected genetic diagnoses are not covered by a single targeted panel or if a targeted panel testing was previously negative

Choose between our smaller, targeted or our comprehensive CentoCancer® panel:

- **Selection of genetic test/panel according to family history and clinical data**
  - BRCA1, BRCA2 panel: 2 genes
  - CentoBreast® panel: 13 genes

- **Complex family history, variability of cancers, and absence of known genetic cause in the family**
  - CentoCancer® panel: 72 genes

For a full list of all available hereditary cancer panels please visit [www.centogene.com](http://www.centogene.com)
CentoMD® is your mutation encyclopedia. Search, select, and filter through genes, transcripts, and variants – generating a detailed description with all associated data tailored to your needs. CentoMD® allows you to diagnose and treat rare diseases in a much more efficient, timely, and targeted manner.

CentoMD® gives clinicians, laboratory experts, and geneticists access to over 12.2 million variants, including variants detected by whole exome and whole genome sequencing. This rapidly growing encyclopedia of genetic, clinical, and epidemiological information is based on fully curated data of individuals from >120 countries. It enables you to increase your diagnostic know-how and cross-reference multiple ethnic backgrounds with gender/age-specific clinical symptoms.

CentoMD® is evidence-based. Every variant within CentoMD® originates from a clinical case analyzed at CENTOGENE, following a highly standardized and accredited workflow.

> 400,000 ANALYZED CASES
> 3,1 B ALLELES IDENTIFIED
> 3,700 ASSOCIATED PHENOTYPES
> 12 M UNIQUE VARIANTS
CENTOMD® 58%* PUBLISHED 42%

* Ratio of newly detected vs. previously published clinically relevant and uncertain variants

All data valid as of December 2019
One-stop solution for diagnostic NGS panels, clinical bioinformatics, & medical interpretation. CentoCloud® is a service specifically designed for human genetic laboratories to support the execution of high-standard next generation sequencing diagnostics. The fully automated bioinformatics pipeline analyzes our customers pre-produced NGS data based on CENTOGENE validated gene panels, annotated with data from our proprietary mutation database (CentoMD®).

HOW IT WORKS:

LOCAL NGS LAB

- Sequencing with CENTOGENE gene panels and ready-to-use protocols

CENTOGENE SERVICES

- Fully-automated bioinformatics solution
- CentoMD® annotation
- Interpretation & reporting (optional)

LOCAL NGS LAB

- Data transfer via FileCloud
- Data transfer via FileCloud
- Information on variant classification & interpretation (reporting optional)

WHAT IT OFFERS:

- Bioinformatics pipeline development and an efficient gene panel design
- Technical & medical consulting - training and mentoring regarding all relevant topics
- Direct access to CentoMD®, what we believe to be the world’s largest and best-curated database of rare genetic disorders
- Workstation setup & validation - if necessary, quality management and accreditation
- Fully validated bioinformatics pipeline
- Comprehensive curation of clinical evidence and interpretation by medical experts
CentoCloud® NGS panel designs are end-to-end validated – driven by CENTOGENE’s medical expertise in clinical diagnostics. The design ensures unique coverage of target regions based on variant information not only from public databases, but also from proprietary CentoMD® that represents information from the largest worldwide cohort of patients with rare diseases.

**PANEL OPTIONS**

CentoCloud® NGS panel designs are end-to-end validated – driven by CENTOGENE’s medical expertise in clinical diagnostics. The design ensures unique coverage of target regions based on variant information not only from public databases, but also from proprietary CentoMD® that represents information from the largest worldwide cohort of patients with rare diseases.

<table>
<thead>
<tr>
<th></th>
<th>CentoCloud® MENDELIOME</th>
<th>CentoCloud® ONCOLOGY</th>
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</thead>
<tbody>
<tr>
<td><strong>Indication</strong></td>
<td>For multiple hereditary diseases. This includes, but is not limited to treatable diseases, early-onset childhood disorders (epilepsies, mental retardation), cardiac disorders, neurodegenerative diseases, skeletal abnormalities, skin diseases, and sensory diseases.</td>
<td>For all relevant hereditary tumor predisposition syndromes, including breast cancer, GI tumors, Li-Fraumeni syndrome, MEN1, MEN2, paragangliomas, and others.</td>
</tr>
<tr>
<td><strong>Genes</strong></td>
<td>2,546 genes, 13Mb target region (v2) CNV analysis available</td>
<td>73 genes, 0.5Mb target region (v2) CNV analysis included</td>
</tr>
<tr>
<td><strong>Coverage</strong></td>
<td>&gt;99% targeted bases at &gt;20x covered</td>
<td>≥99.5% targeted bases at ≥20x covered</td>
</tr>
<tr>
<td></td>
<td>100% coverage of core genes BRCA1, BRCA2, TP53</td>
<td>100% coverage of core genes BRCA1, BRCA2, TP53</td>
</tr>
<tr>
<td><strong>Conditions</strong></td>
<td>Unique gene composition addressing the most relevant indications for genetic testing</td>
<td>Hereditary cancer syndromes</td>
</tr>
<tr>
<td><strong>Patient group</strong></td>
<td>Children and adults with a suspected genetic disorder</td>
<td>Tumor patients and relatives with suspected increased risk of tumors</td>
</tr>
<tr>
<td><strong>TAT</strong></td>
<td>Processing: &lt;5 business days (2 business days for prenatal option) Medical reporting: &lt;2 business days</td>
<td>Processing: &lt;5 business days Medical reporting: &lt;2 business days</td>
</tr>
</tbody>
</table>
CentoPharma® is your tailor-made solution for faster R&D pipelines. The platform provides intelligent access to our comprehensive data repository that combines phenotype, genotype, and biochemistry information with epidemiological data and clinical information from a global cohort originating from more than 120 countries. Dynamic search criteria enables the targeted compilation of individual customized cohorts based on desired geographical region, phenotype, genotype, and suspected or confirmed diagnosis. CentoPharma® is powered by CentoMD®, our unique data repository of rare diseases, including over 12.2 million unique variants. With CentoPharma® users can generate customized datasets ideal for research and drug development – accelerating the discovery and clinical development of orphan drugs.

CENTOPHARMA® IS POWERED BY CENTOMD®, THE WORLD’S LARGEST DATABASE OF RARE DISEASES
CentoMD® is a unique repository of genetic, biochemical and clinical information from over 400,000 consented and curated individuals, including information for more than 3,700 diseases with 14,000 HPO (Human Phenotype Ontology) terms and over 175,000 individuals linked to HPO term(s).
Biomarkers – A Growing Portfolio

CENTOGENE works alongside academic and pharmaceutical partners, as well as patient organizations to develop new diagnostic assays and biomarkers that improve the condition and monitoring of patients affected by hereditary diseases as well as drive orphan drug development.

<table>
<thead>
<tr>
<th>DISORDER COVERED BY CENTOGENE</th>
<th>ENZYMATIC TESTING (ENZYME PANEL)</th>
<th>BIOMARKER TESTING¹</th>
<th>SINGLE GENE ANALYSIS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fabry disease</td>
<td>Alpha-galactosidase (CentoLSD, CentoSphingo®)</td>
<td>Globotriaosylsphingosine (Lyso-Gb3) + others in development¹</td>
<td>GLA</td>
</tr>
<tr>
<td>Farber disease</td>
<td>—</td>
<td>C26-Ceramide</td>
<td>ASAH1</td>
</tr>
<tr>
<td>Gaucher disease type I, II, III</td>
<td>Beta-glucocerebrosidase, Chitotriosidase (CentoLSD, CentoSphingo®)</td>
<td>Glucosylsphingosine (Lyso-Gb1)²</td>
<td>GBA</td>
</tr>
<tr>
<td>Gaucher disease, atypical</td>
<td>—</td>
<td>Glucosylsphingosine (Lyso-Gb1)²</td>
<td>PSAP</td>
</tr>
<tr>
<td>Krabbe disease</td>
<td>Galactocerebrosidase</td>
<td>In development¹</td>
<td>GALC</td>
</tr>
<tr>
<td>Metachromatic Leukodystrophy</td>
<td>Arylsulfatase A</td>
<td>In development¹</td>
<td>ARSA</td>
</tr>
<tr>
<td>Niemann-Pick disease A/B</td>
<td>Acidic sphingomyelinase (CentoLSD, CentoSphingo®)</td>
<td>Lyso-SM-509 &amp; Lyso-SM-465</td>
<td>SMPD1</td>
</tr>
<tr>
<td>Niemann-Pick disease C1/C2</td>
<td>—</td>
<td>Lyso-SM-509 &amp; Lyso-SM-465</td>
<td>NPC1/NPC2</td>
</tr>
<tr>
<td>Aromatic L-amino acid decarboxylase (AADC) deficiency</td>
<td>—</td>
<td>3-O-Methyldopa (3-OMD)</td>
<td>DDC</td>
</tr>
<tr>
<td>Hereditary angioedema (SERPING1 mutation)</td>
<td>—</td>
<td>C4 and C1-INH complement protein, cleaved high-molecular-weight kininogen (cHMWK) + others in development¹</td>
<td>SERPING1</td>
</tr>
<tr>
<td>Transthyretin Amyloidosis</td>
<td>—</td>
<td>In development¹</td>
<td>TTR</td>
</tr>
<tr>
<td>Duchenne</td>
<td>—</td>
<td>In development¹</td>
<td>DMD</td>
</tr>
</tbody>
</table>

¹ Further biomarker developments upon request. Over 30 additional biomarkers, biomarker panels and multi-biomarker patterns in development.
² Lyso-Gb1 has been identified as the most effective biomarker for Gaucher disease (Elstein, Deborah, et al. “Reductions in glucosylsphingosine (lyso-Gb1) in treatment-naïve and previously treated patients receiving velaglucerase alfa for type 1 Gaucher disease: Data from phase 3 clinical trials.” Molecular genetics and metabolism 122.1-2 (2017): 113-120.)
CentoWebinar

Wherever you are, connect with us live, or whenever it suits you, listen to topics you are interested in concerning clinical diagnostic practice and research.

At CENTOGENE, we have established free webinar series (live and on demand) on key developments in clinical diagnostics as well as giving insights into the latest research findings in the field of rare disease.

CentoAcademy®

CENTOGENE’s educational workshop series. Via lecture, seminar and hands-on multi-day courses, clinical scientists and physicians from all over the world are offered the opportunity to learn about:

› Cutting-edge diagnostic technologies
› Global best practices
› Research innovations
› Services

Sharing our knowledge with our partners on-site through seminars and hands-on workshops is the best basis for a solid understanding of complex technological workflows.
Your partner of choice

For further information and support, please contact our closest representative or our customer support team, easily accessible by phone or email.

www.centogene.com

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