Whole Exome Sequencing Panel consent form

GC: .....

NGS Panel Name: .....

In this diagnostic panel, a total of ..... genes known to be associated with the disease ..... are analyzed in a single test. If any pathogenic variants are detected in the mentioned genes, they will be reported. The technology used in this test is Whole Exome Sequencing (WES). WES is a test that detects disease-causing changes in a person's genome by analyzing the protein-coding regions (exons) of genes. This test is different from other genetic tests you may have previously undergone. It focuses on genes that have been reported in the OMIM database to be associated with your condition. It may detect variants in genes directly involved in the proband's condition or novel variants not previously associated with this disease.

To perform the WES test, 5–10 mL of blood is required. DNA will be extracted from the blood sample and subjected to exome sequencing. The individual's DNA sequence will be compared to reference sequences (control/reference genome). A list of potentially pathogenic variants will be generated.

- Due to the complexity and significance of this test, the results should only be interpreted by your physician or a certified genetic counselor. The results will typically be available within 3 to 4 months.
- For many genes, specific screening options and medical recommendations are available. Identification of a pathogenic variant in any of the disease-related genes can help guide precise medical decision-making and individualized recommendations.
- It is important to note that, if positive, the test results can assist in disease management, targeted screening, preventive measures, or supportive therapies where applicable.

Detection of novel variants in the analyzed genes:

If a previously unreported variant is identified that correlates with the patient's phenotype and may explain the disease in the proband, it will be included in the report. However, this does not imply definitive confirmation of pathogenicity.

Molecular genetic test results may be classified as follows:

- Positive: One or more pathogenic/likely pathogenic variants were identified in genes associated with the proband's condition.
- Negative: No pathogenic variants were detected in the analyzed genes.
- Variant of Uncertain Significance (VUS): One or more variants with unclear clinical significance were identified in disease-related genes.
- Unclear: One or more variants were identified that may be clinically/genetically associated with the disease to some extent. Further clinical and genetic investigations are required to assess the pathogenicity of the identified variant(s).

In case variants are identified in additional genes potentially related to your condition, would you like to be informed of them?

☐Yes ☐ No

Please note: Due to the continuous advancement of bioinformatics tools, scientific publications, and clinical guidelines, variant classification is subject to change over time. It is strongly recommended that in case of a future pregnancy, you return to the center for re-evaluation of the results and variant classification.

Secondary Findings:

During WES analysis, incidental (secondary) pathogenic or likely pathogenic variants may be identified in genes unrelated to the primary indication for testing. If such variants are found in genes recommended by the ACMG Secondary Findings list v3.2 (2023), they will be reported as secondary findings. The purpose of reporting these variants is to detect individuals at risk for high-penetrance actionable genetic conditions, for which medical interventions can help prevent or reduce morbidity and mortality.

ACTA2, ACTC1, ACVRL1, APC, APOB, ATP7B, BAG3, BMPR1A, BRCA1, BRCA2, BTD, CACNA1S, CALM1, CALM2, CALM3, CASQ2, COL3A1, DES, DSC2, DSG2, DSP, ENG, FBN1, FLNC, GAA,GLA, HFE, HNF1A, KCNH2, KCNQ1, LDLR, LMNA, MAX, TMEM127, MEN1, MLH1, MSH2, MSH6, MUTYH, MYBPC3, MYH11, MYH7, MYL2, MYL3, NF2, OTC, PALB2, PCSK9, PKP2, PMS2, PRKAG2, PTEN, RB1, RBM20, RET, RPE65, RYR1, RYR2, SCN5A,

SDHAF2, SDHB, SDHC, SDHD, SMAD3, SMAD4, STK11, TGFBR1, TGFBR2, TMEM43, TNNC1, TNNI3, TNNT2, TP53, TPM1, TRDN, TSC1, TSC2, TTN, TTR, VHL, WT1

Would you like to be informed of any secondary findings in these genes if detected?

☐Yes ☐ No

Technical Limitations of the Test:

- Whole Exome Sequencing is performed using Next Generation Sequencing (NGS) technology. NGS has an estimated error rate of 5–10%, hence all potentially pathogenic variants must be confirmed by an orthogonal method.
- NGS cannot reliably detect repetitive regions of the genome (e.g., repeat expansions), such as those involved in Fragile X syndrome, Huntington disease, or Myotonic dystrophy.
- Although the test is designed to identify detectable mutations in the listed genes, large deletions/duplications (CNVs) or variants located in intronic or regulatory regions may not be identified using exome sequencing. Additionally, genes not included in the panel or not yet known to be associated with the disease may be responsible for the condition.

Limitations of Standard Laboratory Testing:

Inaccurate results may arise from the following:

- Poor sample quality
- Lack of access to family member samples
- Inaccurate family history or pedigree
- Incomplete or misleading clinical information
- Technical problems during processing

It has been explained to me/us that the technical results of the performed test may be used for scientific and research purposes, provided that all identifying personal information remains confidential. I/we hereby give my/our consent for such use.

Furthermore, it has been clarified that the laboratory is obligated to provide technical information to national authorities upon request, in accordance with the regulations approved by the Ministry of Health.

I/we, the undersigned, after reading all the points mentioned in this consent form, receiving adequate explanations, and having had sufficient opportunity to ask questions, knowingly and voluntarily—without any coercion or pressure—and with full awareness of the possible outcomes of the aforementioned tests and their potential emotional, psychological, or physical consequences, hereby sign this consent form and request the laboratory to proceed with the test.

I, as the patient or the patient's legal representative, authorize the use of the blood sample for this panel. I understand that once the test has been accepted, it cannot be cancelled.

☐ I hereby consent to the performance of molecular genetic testing.

Patient Name: ..... Signature & Date:

Parent/Legal Guardian Name (with relation): ..... Signature & Date:

Witness Name: ..... Signature & Date: