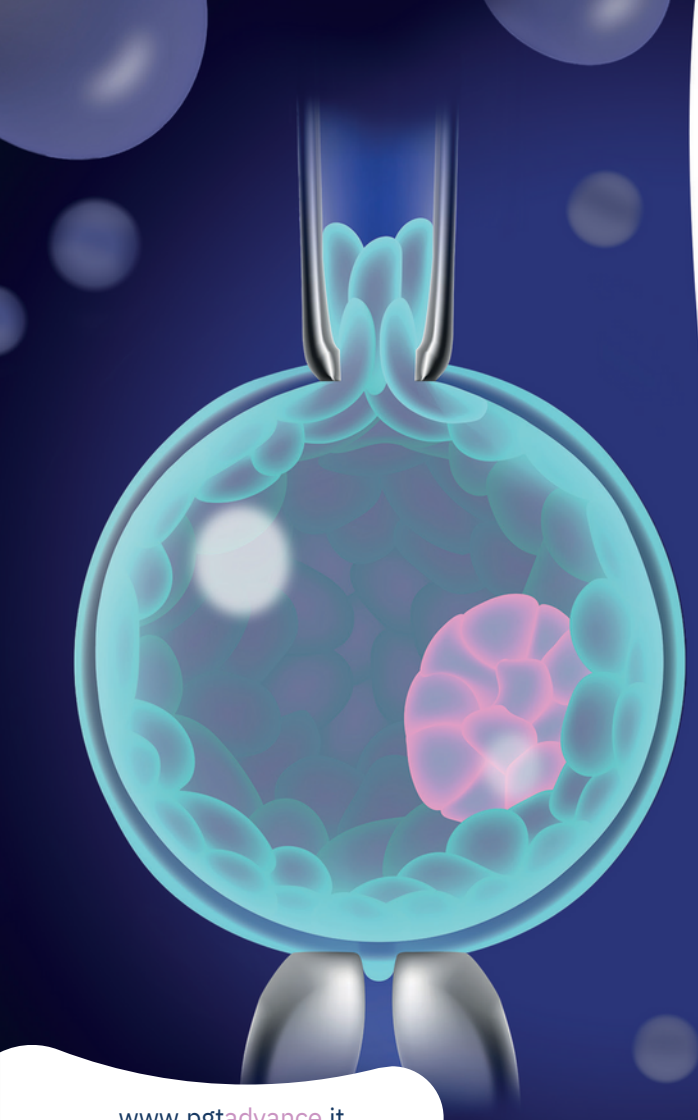
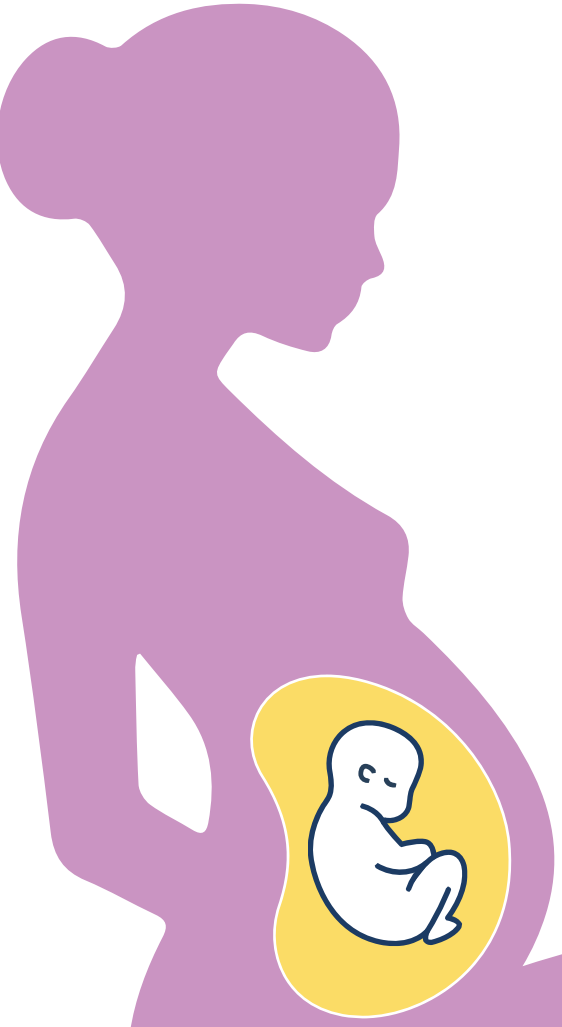


GENOMICA
Next Generation Genetics

Advanced strategies for detection of genetic disorders and chromosomal abnormalities in embryos

PGTADVANCE
NEXT GENERATION PGT

www.pgtadvance.it



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PREIMPLANTATION GENETIC TESTING (PGT)

Couples who are carriers of genetic disorders, including recessive or dominant single gene defects, sex-linked conditions, or chromosome rearrangements, face a reproductive risk: affected pregnancies may result in miscarriage or in the birth of a child with significant phenotypic abnormality, sometimes resulting in early death.

Such couples have the option of undergoing prenatal diagnosis once a pregnancy is established, either by amniocentesis or chorionic villus sampling (CVS), to allow the detection of the genetic disorder in the fetus. However, with these procedures, if a genetic abnormality is detected, parents may face the difficult decision of whether or not to continue the pregnancy.

PGTADVANCE
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A GROUNDBREAKING TECHNOLOGY TO IDENTIFY GENETIC DEFECTS IN IVF EMBRYOS

Preimplantation genetic testing (PGT) has been introduced as a technique complementary to prenatal diagnosis in order to increase the options available for at risk couples. Its intended goal is to significantly reduce a couple's risk of transmitting a genetic disorder or a chromosomal abnormality by diagnosing such conditions in oocytes or early human embryos that have been cultured in vitro, before a clinical pregnancy has been established. After testing, only embryos diagnosed as unaffected are selected for transfer to the woman's uterus.

The great advantage of PGT over prenatal diagnosis is that a potential termination of pregnancy is avoided. This gives couples the opportunity to start a pregnancy with the knowledge that their child will be unaffected. Consequently, PGT does not require a decision regarding possible pregnancy termination.

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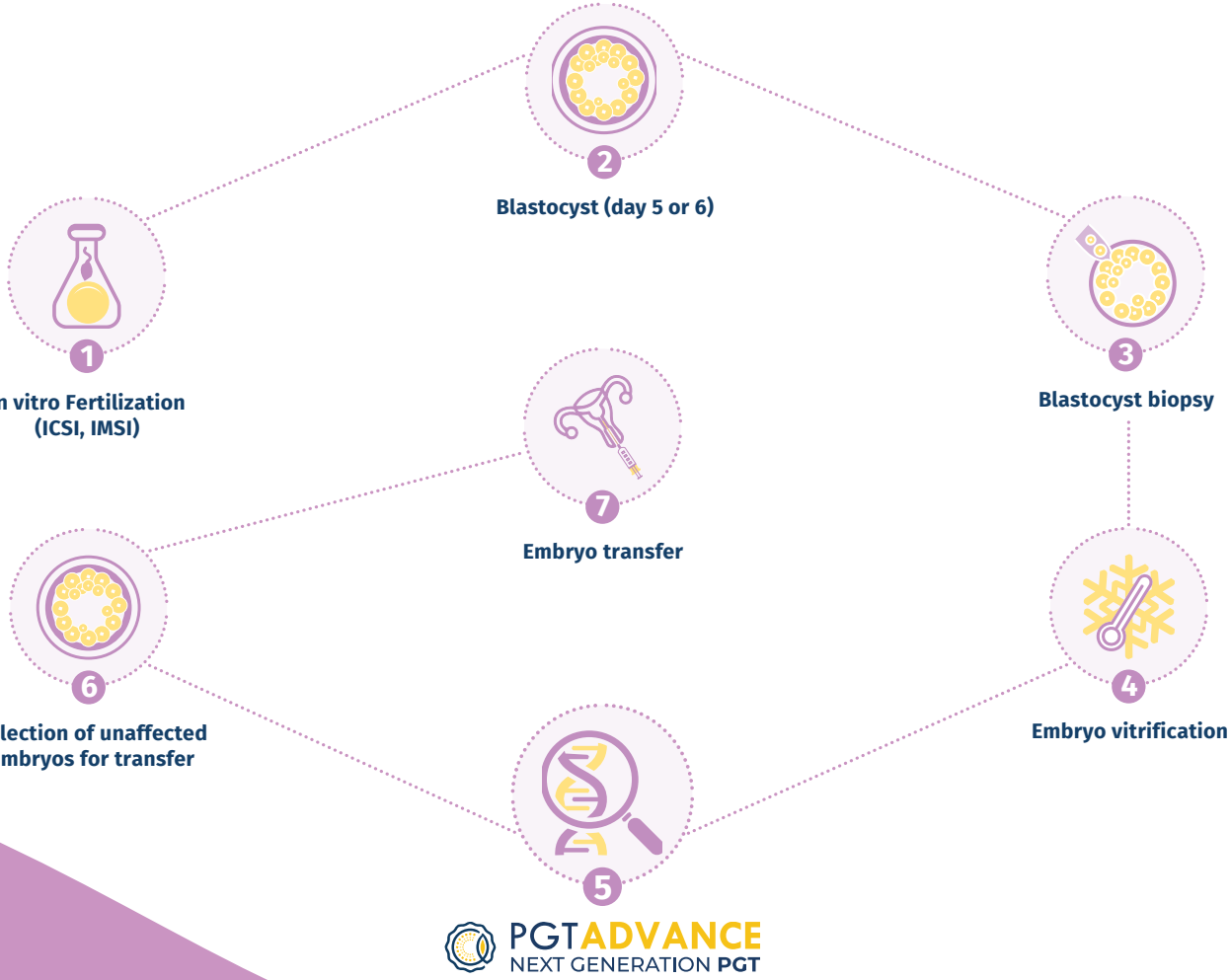
PGT PROCEDURE

PGT usually requires that the couple undergoes to an in vitro fertilization (IVF) treatment **(1)**.

This involves hormonal treatments that allow the collection of multiple eggs from the mother. The eggs are then fertilized using the father's seminal fluid and the resulting embryos are transferred to an incubator. After five or six days the embryos usually consist of a tiny ball of a couple hundred cells (blastomeres), known as blastocyst **(2)**. To test the blastocyst, an opening is made in the covering of the embryo. Blastomeres are then removed (biopsied) from trophectoderm of each embryo **(3)** and subjected to genetic testing **(5)**.

Then, all embryos will be frozen **(4)** and will remain at the IVF center for a future frozen embryo transfer. If blastomeres are found to be unaffected by the specific genetic condition then the embryo that it was removed from will also be unaffected. Embryos that are revealed to be healthy **(6)** can be transferred to the womb **(7)**, ultimately producing unaffected babies.


1
In vitro Fertilization
(ICSI, IMSI)
2
Blastocyst (day 5 or 6)
3
Blastocyst biopsy
4
Embryo vitrification
5
6
Selection of unaffected
embryos for transfer
7
Embryo transfer
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PGTADVANCE
NEXT GENERATION PGT

A CUTTING-EDGE TEST THAT OFFERS A FULL PANEL OF SCREENING OPTIONS

PGTADVANCE A

PGT-A **Preimplantation genetic testing for chromosomal aneuploidy (PGT-A)**

Preimplantation genetic testing for chromosomal aneuploidy (PGT-A) is a technique used in conjunction with In-Vitro fertilization (IVF) to detect embryos with extra or missing chromosomes (aneuploidy). An extra chromosome is known as a "trisomy" and a missing chromosome is known as "monosomy".

Through PGT-A, the selection of embryos to be transferred to the uterus is based not only on a morphological evaluation but also on the related chromosomal ploidy, which reflects their possibility of giving rise to an ongoing pregnancy.

Embryos that are affected by certain chromosomal conditions can lead to failure of implantation, pregnancy loss, or result in the birth of a child with physical and/or mental problems. The purpose of PGT-A is to help prevent adverse outcomes by identifying affected embryos in the laboratory and preventing them from being transferred into the uterus.
PGT-A can help in the selection of chromosomally normal embryos for transfer in order to increase the chance of pregnancy, reduce the chance of miscarriage, and reduce the chance of children born with medical conditions.

PGT-SR

PGTADVANCE SR

Preimplantation genetic testing for structural chromosomal rearrangements (PGT-SR)

Preimplantation Genetic Testing for Structural Rearrangements (PGT-SR) is offered to patients who, before IVF treatment, find out that one of the partners is a carrier of a balanced structural rearrangement, such as a translocation or inversion.

The carriers of balanced structural rearrangements present abnormalities in the structure of the chromosomes, without gains or losses in chromosomal material. The risk factors of being a carrier of a balanced translocation or inversion include unexplained male infertility (low sperm count), implantation failure, recurring miscarriages, and family history of having offspring born with abnormalities.

In carriers of balanced structural rearrangements, there is a risk of producing eggs and sperm with unbalanced chromosomal alterations which could be transmitted to the offspring. In general, a carrier of a balanced structural rearrangement does not have health problems, although in some cases they may have difficulty conceiving. The embryos of carriers of balanced structural rearrangements may present unbalanced structural rearrangements (gain or loss of a chromosome segment), which may lead to implantation failure, miscarriage, or children born with mental and/or physical problems. If the children inherit the balanced structural rearrangement, they should not have health problems, just like their carrier parent(s).

The identification of embryos which have inherited an unbalanced structural rearrangement may help patients and clinicians to decide which embryos to transfer.

PGT-M

PGTADVANCE M

Preimplantation genetic testing for monogenic disorders

Couples who are carriers of genetic disorders, including recessive or dominant single gene defects or sex-linked conditions, face a reproductive risk. For patients at risk of passing on a dominant disorder to their children, natural conception usually carries a 50% chance with each pregnancy that the fetus will be affected by the disease. Couples where both parents are carriers of a recessive disorder generally face a 25% chance with each pregnancy of having an affected child.

Preimplantation genetic diagnosis (PGT-M) significantly reduce a couple's risk of transmitting a genetic disorder by diagnosing a specific genetic disease in oocytes or early human embryos that have been cultured in vitro, before a clinical pregnancy has been established.

Since PGT-M is performed on single or a few cells, the genetic analysis technique has to be adapted and pushed to its physical limits. This implies first the design and development of the PGT-M strategy, followed by a process of fine-tuning of the analysis conditions on single cells, in order to optimize and validate the PGT-M protocol before its clinical application. This phase is known as "**pre-clinical PGT-M work-up**".

The pre-clinical PGT-M work-up includes blood sample and/or cheek cells analysis of the prospective parents for mutation verification and informativeness testing for the polymorphic markers included in each assay.

Almost all genetically inherited conditions that are diagnosed in the prenatally can also be detected by PGT-M. Generally, it is possible to perform PGT-M for any genetic disorders, autosomal dominant, recessive or X-linked, with an identifiable gene.

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INDICATIONS FOR TESTING

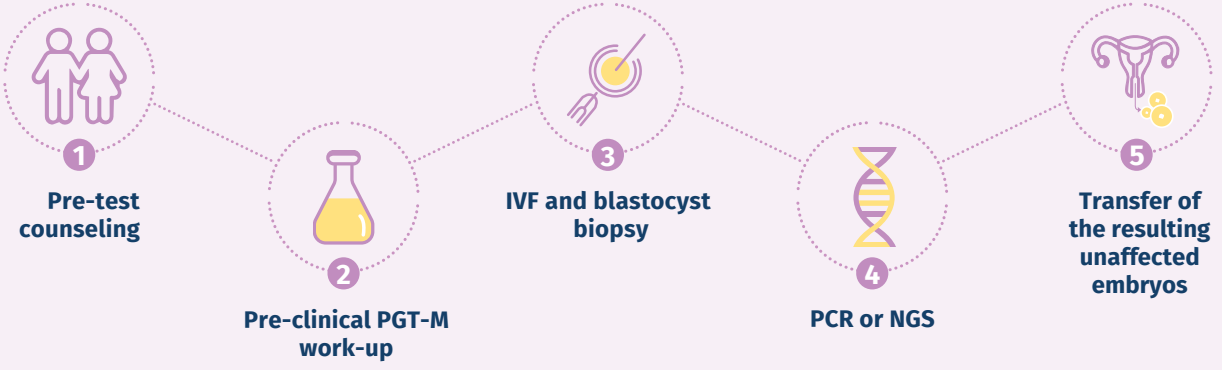
	INDICATIONS	AIMS	BENEFITS
 PGT-M	• Couples who are carriers of genetically transmittable genetic disorders	Detection of a genetic disorder in oocytes or IVF-derived human embryos	It drastically reduce the risk of transferring an embryo affected by a specific genetic disease.
 PGT-SR	• Couples who are carriers of a balanced structural rearrangement	Detection of unbalanced structural chromosomal abnormalities in oocytes or IVF-derived human embryos	It drastically reduce the risk of transferring an embryo affected by an unbalanced structural chromosomal abnormality.
 PGT-A	• Advanced maternal age (AMA); • Recurrent miscarriages (RM); • Repeated implantation failure (RIF); • Severe male infertility (Azoospermia);	Detection of chromosomal aneuploidies in IVF-derived human embryos	• identification of embryos that are affected by chromosomal aneuploidy; • increasing the chance of pregnancy; • reducing the chance of miscarriage; • reducing the chance of children born with medical conditions.

PGTADVANCE
NEXT GENERATION PGT

GROUNDBREAKING TECHNOLOGIES AND HIGH QUALITY STANDARDS

PGTADVANCE M

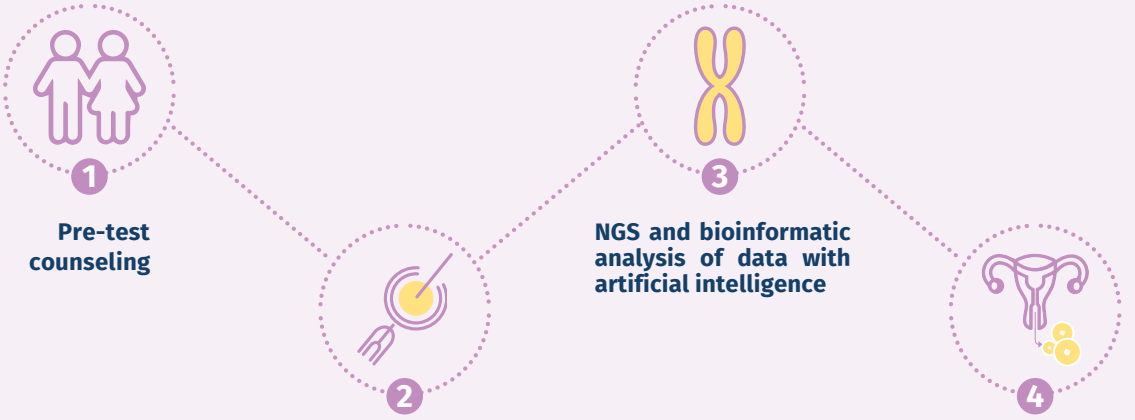
A genetic test designed to identify in embryos mutations causing genetic disorders



PGTADVANCE A

PGTADVANCE SR

A genetic test designed to identify in embryos chromosomal aneuploidy and unbalanced structural abnormalities



PGTADVANCE *Plus*

THE EVOLUTION OF PGT

The **PGTADVANCE *Plus*** tests are integrated with the **Next Generation Sequencing** (**NGS**) analysis of numerous variants in the embryonic DNA sequence, known as **single nucleotide polymorphisms (SNPs)**.
This test, through the use of a sophisticated bioinformatic analysis allows:

- the identification of **triploidy** (which affect **~2-3%** of pregnancies and is responsible for **~15-18%** of miscarriages) and **haploidy**, chromosomal anomalies not detectable with standard PGT-A techniques;
- to carry out a **quality control** of the results aimed at:
  - detection of potential contaminations deriving from cumulus cell DNA;
  - prevention of **sample mix-ups** through identification of genetically related embryos.

PGTADVANCE
NEXT GENERATION PGT

NON-INVASIVE PGT:
THE NEXT LEVEL IN PREIMPLANTATION GENETIC TESTING

EMBRYOADVANCE

Non-Invasive PGT by analysis of cell-free embryonic DNA in spent culture medium

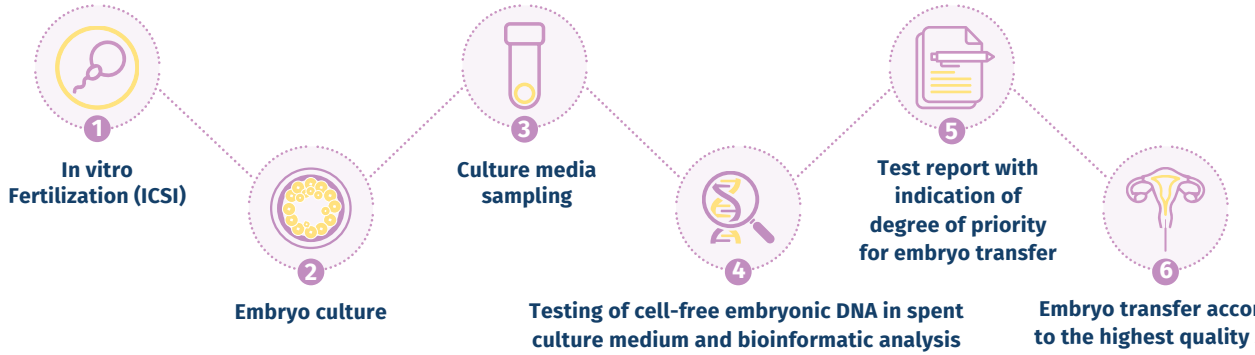
A pioneering non-invasive pre-implantation genetic test that allows identification of embryos with a higher probability of euploidy, and therefore with a higher implantation potential, by analyzing the cell-free embryonic DNA in spent culture media.
EmbryoAdvance test assigns the embryos a degree of priority for transfer to the uterus, based on information on the chromosome copy number of the embryos. This information may be used for selecting optimal embryo to prioritize and transfer first in an IVF cycle, thus maximizing the chances of success of the IVF treatments.

BENEFITS

- Improving the effectiveness of IVF techniques in groups of patients characterized by reduced reproductive performance;
- Reducing the time to pregnancy;
- Reducing the risk of spontaneous miscarriages, related with the presence of chromosomal abnormalities in the embryo

EMBRYOADVANCE

NON-INVASIVE PGT PROCEDURE



IVF derived embryos, during their in-vitro development, naturally release into the culture medium DNA fragments, named **embryonic DNA**, with higher concentrations as the number of cells increases with the embryo development at blastocyst stage. This feature allows, through the use of state-of-the-art instrumental technologies, to assess the embryonic chromosome copy number in a non-invasive manner, without the need to perform the trophectoderm biopsy.

The EmbryoAdvance test analyzes the cell-free embryonic DNA released into the culture medium during the development of the embryo, using Next Generation Sequencing (NGS) technologies and advanced bioinformatics analyses. The test is performed by collecting a sample of embryo culture medium by the embryologists of the IVF center, carried out on day 6 or day 7 of development. Subsequently, the chromosomal regions of embryonic DNA are sequenced using NGS sequencers. The chromosomal sequences are then quantified through an advanced bioinformatic analysis, in order to detect embryonic chromosomal aneuploidies, identified by a greater amount of embryonic sequences relating to a specific chromosome as compared to a "normal" reference standard. A proprietary algorithm will allow to obtain a quality score for each embryo and therefore a degree of priority (High, Medium, Low) for its transfer to the uterus.

PGTADVANCE
NEXT GENERATION PGT

BENEFITS

- Possibility of combining PGT-M/SR with PGT-A
- **Personalized Genetic couseling** with genetic counselors experts in PGT
- State-of-the-art technologies (NGS)
- Personalized set-up
- Accuracy 99%
- Possibility to perform preimplantation HLA matching

Fast TAT: 7-10 days

SHIPPING KIT

The box contains all necessary consumables/reagents for transportation of biopsied embryonic cells.

GENOMICA
Next Generation Genetics

Advanced molecular diagnostics solutions using state-of-the art technologies

GENOMICA is recognized as one of the most advanced molecular diagnostics laboratory in Europe, both for the state-of-the-art instruments and technologies, as well as for its high quality standards.

With a **comprehensive portfolio of over 10.000 genetic tests,** GENOMICA is able to satisfy increasingly specialised requests in the field of molecular genetics, providing physicians and their patients with innovative and highly specialised diagnostic solutions for any clinical need.

Over **100.000** genetic tests/year

Professionals with 20+ years experience in the field of genetics and prenatal molecular diagnostics

Personalized genetic counseling with genetic counselors experts in discussing genetic test results and familial risks

Test performed in Italy (Rome or Milan)

Fast TAT

Laboratories with **groundbreaking technologies** and high quality standards

International **Partnerships**

Dedicated R&D team

LABORATORIES

Rome: Via Arduino 38 - 00162 - Tel.: +39 06.21115020
Milan: Viale L. Bodio 29-37 (Bodio 3) - 20158 - Tel.: +39 02.21115330
E-mail: info@genomicalab.it - **www.genomicalab.it**

REGISTERED OFFICE

Rome: Via Arduino 38 - 00162
Pec: info@pec.genomicalab.it
VAT no.: 14554101007 - REA: RM - 1530210

PGTAdvance M eng rev. 01