SCOLI

For Adolescent Idiopathic Scoliosis

SCOLI GEN — Early detection

SCOLI MIR — Diagnosis & Prognosis

SCOLI VIEW — Monitoring & Management

SCOLI

For Adolescent Idiopathic Scoliosis

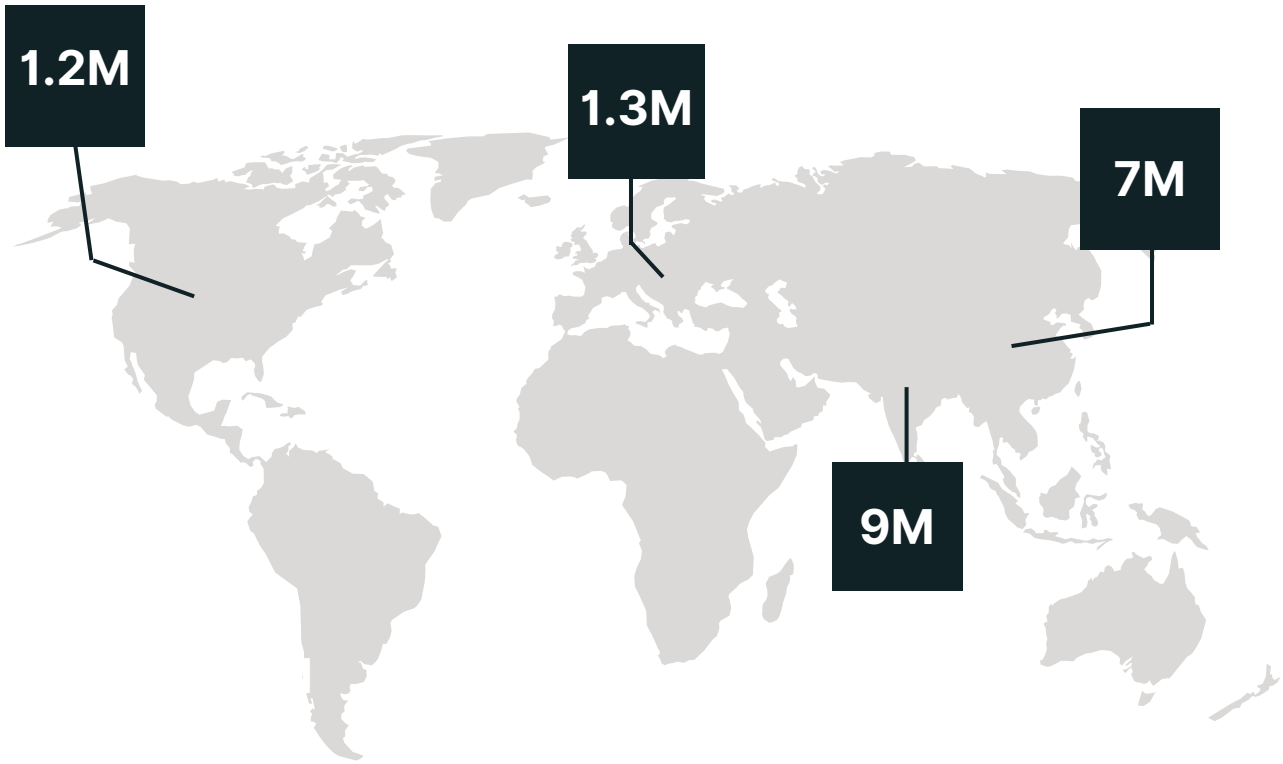
Adolescent Idiopathic Scoliosis (AIS) is a three-dimensional spine deformity, with a progressive natural history in some patients that can reach severe spine curves producing painful spinal osteoarthritis. It affects 20 million adolescents between the ages of 10-17 years old globally. AIS has an estimated incidence of between 3% of new births globally.

Currently there are no tools available to allow the early detection of AIS, before gross clinical symptoms become apparent.

There is also a lack of prognostic tools for AIS treatment planning and management. This creates a situation where a **"wait and see"** approach is adopted, with AIS detected late in its evolution, resulting in the sub-optimum use of resources and clinical outcomes for patients.

In response to this unmet medical need EpiDisease has developed three precision products to **identify before symptoms appear children** with a **high risk of developing AIS** (***ScoliGEN***), to **diagnose at a molecular level which children have AIS** (***ScoliMIR***), and to **robustly measure the degree of spine curvature** (***ScoliVIEW***).

The synergistic use of this portfolio will be disruptive to the treatment of AIS. It will allow clinicians for the first time to make precision and data-based pre-emptive clinical decisions throughout the AIS patient journey, from early detection to possible spinal surgery.



AIS Global Cases

The prevalence worldwide of AIS ranges from 0.35% to 13%, depending on ethnicity, gender, and screening methods, with the condition being more common among females than males.

AIS has an impact on the child's development not just physically but also psychologically, emotionally, and mentally

Our Products

The ScoliGEN test indicates the risk of developing AIS. It is based on the analysis of a panel of 20 Single Nucleotide Polymorphisms (SNPs) located in genes identified in peer reviewed scientific publications as being associated with the risk of AIS disease onset and progression.

The test only needs to be performed once per patient and it can be carried out at any time during the subject´s life, even if the subject does not have overt clinical symptoms of AIS.

DNA is obtained from a saliva sample, and after DNA and bioinformatic analysis, a ***Polygenic Risk Score (PRS)*** is calculated using proprietary algorithms that indicates the **subject´s risk of developing AIS** based on its personalised genetic background.

ScoliGEN has a Sensitivity (Sn) of 90% and Specificity (Sp) of 39%, a Positive Predictive Value (PPV) of 56% and a Negative Predictive Value (NPV) of 82% making it an ideal **early AIS triage tool for discounting children who will not devlop AIS**.

ScoliGEN is a robust clinical decision-making support tool, helping clinicians provide personalised and precision care, avoid unnecessary costs and erroneous referrals to specialised AIS clinics [1].

[1] Meirick T, Shah AS, Dolan LA, Weinstein SL. Iowa Orthop J. 2019;39(1):57-61. PMID: 31413675; PMCID: PMC6604530.

SCOLI GEN

110 subjects tested

Sensitivity (Sn) 90%

Specificity (Sp) 39%

Negative Predictive Value (PPV) 82%

Positive Predictive Value (NPV) 56%

User Case

ScoliGEN can be used pre-emptively at the very earliest suspicion of AIS, even **BEFORE** clinical symptoms are apparent. This situation could arise in a child born to parent who had a diagnosis of AIS, or the younger sibling of a child who already has a diagnosis of AIS.

ScoliGEN allows for the dectection of the at-risk patient population, allowing the timely and efficient allocation of resources to those children that most need them.

The high sensitivity and NPV of ScoliGEN combines synergistically with the Adam´s test already incorporated into international pediatric revision protocols to form an efficient and effective combined screening tool for the pediatric population.

Current development status

- **A polygenetic risk score (PRS) algorithm for AIS risk has been developed and validated in a cohort of 110 subjects,**
- **EpiDisease will market the test as a laboratory developed test (LDT)) to accelerate patient's access to this disruptive tool,**
- **ISO 13485 standard for the management of the manufacture of ScolGEN IVD test has been implemented, and its licensing for manufacture is expected in 2026,**
- **A clinical performance trail the leading AIS center in Kolcata (india) will test 300 AIS patients and control individuals has started in 3Q2025 and will run for 24 months.**

Our Products

ScoliMIR is an IVD epigenetic test that supports AIS clinical specialists data-based decision making regarding disease diagnosis. severity, risk of progression, and responsiveness to conservative treatment interventions such as bracing and physiotherapy.

ScoliMIR measures the dynamic nature of a panel of microRNAs in peripheral blood samples [2] related to AIS evolution using quantitative polymerase chain reaction techniques (qPCR).

This data generated by the test is used in proprietary algorithms to calculate a **Scoliosis Risk Index (SRI)**, which predicts the risk of scoliosis progression to more severe deformity.

As a diganostic tool ***ScoliMIR*** has a Sensitivity (Sn) of 96%, a Specificity (Sp) of 86%, a Positive Predictive Value (PPV) of 95% and a Negative Predictive Value (NPV) of 92%.

As more data regarding AIS patients is added to the ScoliMIR predictive model these values will improve, making the tool even more robust and valuable as a support tool for personalised and data driven clinical decision making.

[2] García-Giménez JL., et al. Scientific Reports. 2017. 8(1):2646

SCOLI MIR

80 subjects tested

Sensitivity (Sn) 96%
Specificity (Sp) 86%
Positive Predictive Value (PPV) 95%
Negative Predictive Value (NPV) 92%

The patent for this technology was granted in Europe (nº EP3 310 926), Hong Kong (nº HK1253908), the USA (nº 15/736,735), China (Numb. 201680048488.2), and Canada (2,989,480) providing wide patent protection across key strategic markets with an estimated Total Available Market (TAM) of 10 million AIS patients.

User Case

As an epigenetic biomarker tool, ScoliMIR can provide a diagnosis of AIS from a blood sample even before overt clinical signs are evident.

Upon suspicion of AIS, whether from a positive Adam's test, a first X-ray indicating spinal curvature, or a ***ScoliGEN*** *test result indicating a high risk of AIS,* ***ScoliMIR*** *can provide a definitive diagnosis of AIS with a high level of accuracy.*

The ***ScoliMIR*** *test results can be used for data-driven clinical decision making, allowing for preemptive planning of AIS management and advancing the clinician ahead of the evolving AIS curve.*

Current development status

- **The prototype *ScoliMIR* kit has been validated in a clinical performance utility trial of 50 patients,**
- **A strong and active network of clinical key opinion leaders in the area of AIS, as well as Institutional relationships with patient associations, has been formed by EpiDisease, and a strategy for marketing *ScoliMIR* to these groups has been developed.**

Our Products

SCOLI VIEW

During the clinical trials carried out for the development of ***ScoliMIR***, investigators at EpiDisease noted and explored the concerns of physicians managing AIS patients.

One of these concerns related to problems with the robust and replicable measurement of the **Cobb angle**, a fundamental clinical metric of spinal curvature used to monitor the evolution of AIS, and an important variable used to decide the timing for possible surgical spine correctional procedures.

This classical metric is currently measured using a manual procedure by AIS physician specialists, which is very subjective, and results in a high degree of intra- and inter-user error [3].

In recognition of the high degree of variability in this measurement procedure, clinical guidelines recommend that the Cobb angle should be calculated from the measurements of three different clinicians. However, in practice there is often no time, or available resources, to properly execute and follow the guideline´s recommendations.

Additionally, the variability in the Cobb angle measurement prevents the measurements taken by one health provider being used by a different health provider. This means that if a patient changes hospital, another X ray series must be taken, exposing the patient to an additional dose of ionising radiation.

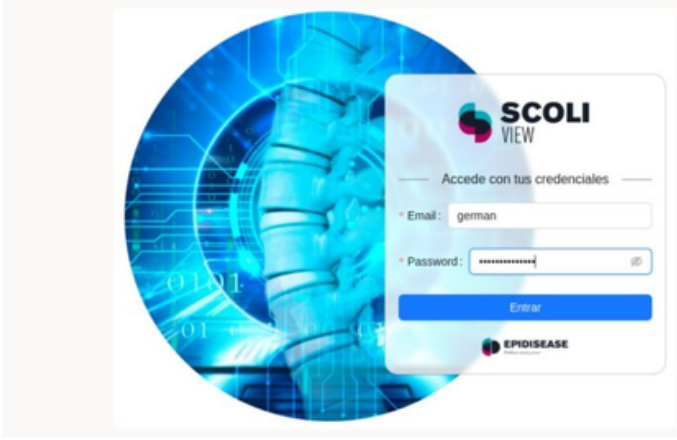
An increase of cancers has been reported in AIS patients that may be linked with their more frequent exposure to radiation, and there is thus a requirement to reduce the number of X rays taken of AIS patient´s spines too monitor their evolution [4].

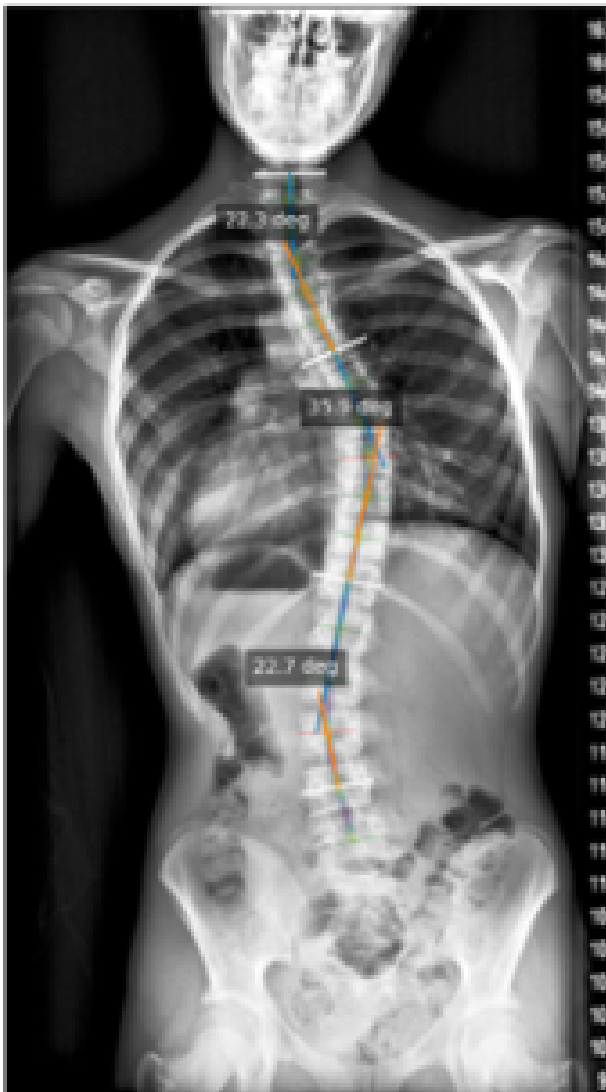
[3] José Hurtado-Avilés,et al. Int J Environ Res Public Health. 2022 Apr; 19(8): 4655
[4] Ane Simony et al, Eur Spine J . 2016 Oct;25(10):3366-3370

In response to these needs EpiDisease has developed ***ScoliVIEW*** **a stand-alone image analysis software capable of automatically measuring the Cobb angle from a standard radiograph with minimal user input.**

The utility and value of this software will be further enhanced by the application of artificial intelligence algorithms to further improve the protocols of patient follow-up, appropriate scheduling of Hospital visits, and support for decision making regarding the optimum treatment based on the use of bracing.

ScoliVIEW data could even support the physician´s decision to anticipate spine surgery by the identification of patients with high risk of progression, and a predicted poor response to conservative treatment protocols, such as bracing.





Current development status

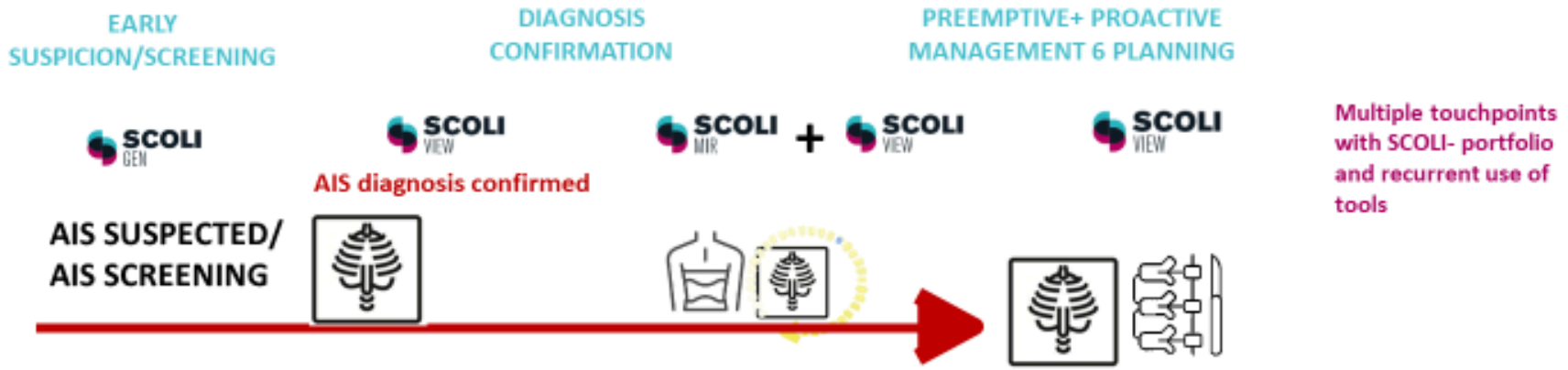
- The *ScoliVIEW* software prototype has been developed and validated in a clinical performance utility trial of 50 patients,

- EpiDisease is the beneficiary of 488.564€ from a public-private collaboration project with a total grant of 610.706€ from the Ministry of Economic Affairs and Digital Transformation (Spanish Government) through RED.es program and NextGeneration EU funding to develop the project titled "Development of a diagnostic technology based on computational image analysis with integration of epigenetic biomarkers for precision medicine in idiopathic scoliosis (ScoliVIEW) (Ref. Numb. 2021/C005/00153042)". The aims of this project are:

  - to improve the *ScoliVIEW* software and associated algorithm with a high number of X-ray images,
  - to combine molecular data (i.e., epigenetic biomarkers based on miRNAs), clinical data, and data obtained from through radiomics-based analysis to identify patients with the highest risk of disease progression,
  - to identify those patients who can benefit from the use of braces, as well as to predict those patients who have finally undergone surgery.

- *ScoliVIEW* has been validated in 1500 images a mutlicentric clinical performance trial in Spain. It is now available for commercial use as a RUO tool.
- A usability trial hasbeen performed in 4Q25.
- CE certification of ScoliVIEW is expected in 1Q26.

Patient pathway with the SCOLI- portfolio



AIS risk status detected early

AIS false positives reduced
Efficient use of resources

Optimised and precise treatment leads to:
Better clinical outcomes
Healthcare savings

Fewer X rays needed

Regulatory status

PRS algorithm validated in 250 subjects

LDT granted under ISO15189 standard

Certification underway and expected in 2025

A performance trial in leading AIS centers in Spain will test 250 additional AIS patients and control individuals

4Q2024-4Q2026

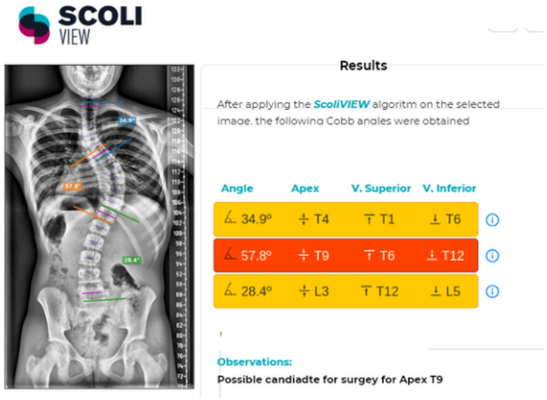
SCOLI GEN

Diagnostic algorithm developed and validated in 1500 X rays

ROU currently

Certification underway and expected in 2025

4Q2024-4Q2026



About Us

EpiDisease S.L. (EpiDisease, www.epidisease.com) is an epigenetics biotechnology company that was founded in 2014 which develops and commercialises a pipeline of patented proprietary in vitro diagnostic (IVD) products and clinical software tools incorporating AI for complex human diseases.

EpiDisease has internationally recognised expertise in the analysis of epigenetic mechanisms such as DNA methylation, histone code/variants and miRNA, which are crucial for the study of gene expression. The Company has developed proprietary models for the development of novel epigenetic biomarkers and has characterized epigenetic drugs for public and private clients.

EpiDisease is a spin-off of the Centre for Biomedical Network Research (CIBER) of the Spanish National Institute of Health Carlos III (ISCIII) (), and is a Spin-Off of the Biomedical Research Institute INCLIVA and the University of Valencia

EpiDisease was recognosed as an innovative company by the Spanish Ministry of Economy in 2017, and this seal was renewed in 2020.



EpiDisease has been certified as Clinical Diagnostic Center in Genetics and Microbiology by the Consellería de Salut Pública i Sanitat Universal- Generalitat Valenciana (Registry No. 22325).

The Company obtained recognition as support center for COVID-19 PCR testing by the Spanish Ministry of Science and Innovation through the Spanish Institute of Health Carlos III and in July 2021 obtained the ISO 9001:2015 quality management certification as a COVID diagnostic laboratory.

EpiDisease has implemented the ISO 13485 standard for the management of the manufacture of medical devices, and ISO15189:2022, standard that establishes requirements for quality and competence in medical laboratory. The acrediation of both standards in expected in 2026.

EPIDISEASE

Unlocking Tomorrow's Health with Epigenetic IVD Tools Today

EpiDisease receives support from the Valencian,Spanish and EU governments

Our Partners